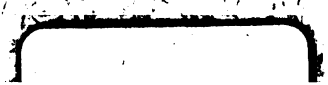

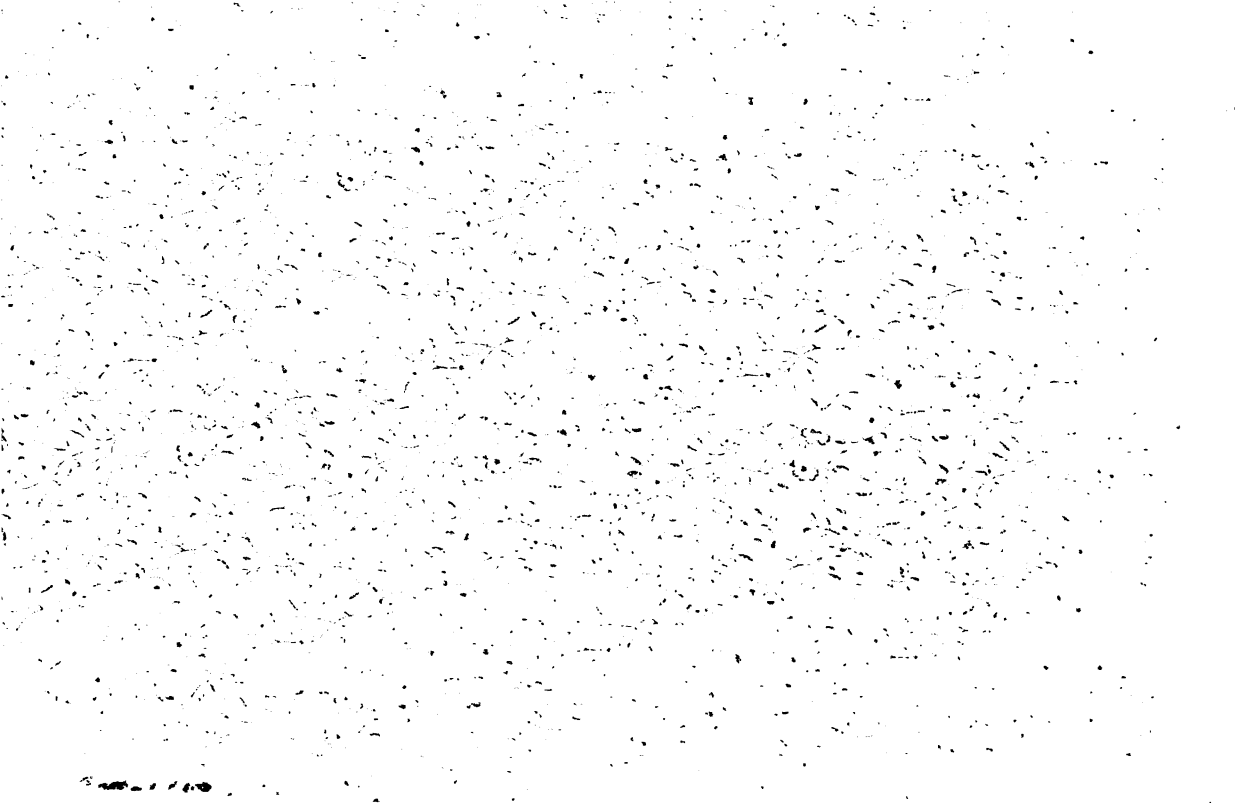

Dr. M. F. Gavin

with kind regards

of The Author.

# A GUIDE

TO

# THE CLINICAL EXAMINATION

OF

# THE URINE.

BY

FARRINGTON H. WHIPPLE, A.B. (HARV.).

BOSTON:
DAMRELL AND UPHAM,
The Old Corner Bookstore,
283 WASHINGTON, CORNER SCHOOL STREET.
1891.

University Press:
John Wilson and Son, Cambridge.

TO

My Respected Instructor,

EDWARD S. WOOD, A.M., M.D.,

THIS VOLUME IS DEDICATED

By The Author.

# PREFACE.

IT has been my aim in writing this little book merely to condense the essential features of larger and more diffuse works, and thus to present the subject in a more readily accessible and practical form. My hope is that the exposition has been as clear as is consistent with its brevity, and that the unavoidable repetition of many facts may serve to indicate their importance and facilitate their retention by the student.

I am indebted for my facts to Dr. Wood of the Harvard Medical School, and also to the works of Roberts, Hoffmann and Ultzmann, Tyson, Birch-Hirschfeld, and Foster.

To my friend and classmate, E. W. Taylor, thanks are due for his assistance with regard to the mechanical details connected with the preparation of the work.

F. H. W.

BOSTON, Jan. 20, 1891.

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# A GUIDE

TO THE

# CLINICAL EXAMINATION OF THE URINE.

## INTRODUCTION.

THE processes of body metabolism are, on the one hand, constructive or anabolic, and on the other, destructive (retrograde) or katabolic. The products of the former, inasmuch as they are of service to the body in maintaining its vital functions are, in many instances, termed secretions, whereas the latter, inasmuch as they can no longer be of service to the living organism, and because the body strives to get rid of them, are called excretions. Speaking broadly, the excretions may be considered to be water, urea, carbon dioxide, and various organic and inorganic salts. Of these the lungs eliminate carbon dioxide and some water, the skin a considerable amount of water, some carbon dioxide, and an insignificant proportion of the salts, while the kidneys remove a very large amount of water, urea, its allied

compounds, and most of the salts. Since these represent the final products of metabolism and under conditions of health are tolerably constant in appearance, composition, and amount, it would seem perfectly rational to examine them if it is desirable to know the probable condition of those vital processes of which the excreta are a product. Of the excreta, the urine offers greatest facilities for examination, and from it the most useful information is obtained.

The healthy urine, then, is a normal product of katabolism, depending for its continual production and in general unvarying composition, on the one hand, to the uninterrupted processes of tissue metamorphosis, and, on the other, to a physiological and anatomical intactness of the kidney itself. The examination of the urine, therefore, not only shows the general condition of body metabolism (i. e. rapidity of the vital processes) and of the kidneys (i. e. their functional activity), but, inasmuch as the urine passes, on its way out of the body, through a series of passages varying in structure and physiological function, it bears witness to the condition of these as well.

The most valuable information that the examination of the urine gives is that which relates, in the first place, to the condition of the kidney and its capacity for work, and in the second, to the state

of the channels by which the urine leaves the body. A knowledge of these facts is of great value, not only in interpreting disease, but also in furnishing grounds upon which to base a prognosis and the proper plan of treatment.

Before passing to the consideration of the urine itself, it may be well to review briefly the nature of the process by which the kidney performs its work.

In the first place there is the theory of Bowman, in which the separation of the urine is regarded as partly one of filtration and partly one of elaboration. Certainly the long and tortuous tubuli uriniferi, with their wealth of epithelium and intimate relation to the capillary loops, suggest the probability of epithelial elaboration, while the Malpighian corpuscle, with its thin and insignificant layer of epithelium enveloping the tortuous knot of capillaries and the immediate connection of the latter with the renal artery where the pressure is tolerably high, suggests separation under pressure, i. e. a kind of filtration.

In the second place there is the theory of Ludwig. According to his view, the separation is one of simple osmosis. The blood, drained, in the glomeruli, of much of its water, passes in a thickened state to the capillaries surrounding the convoluted tubes. Here the conditions for osmosis

are perfect, — two fluids of different densities on either side of an animal membrane; the thin watery fluid that has descended from the Malpighian bodies is in the tubes, while the thickened blood, separated from the former by the capillary wall, the basement membrane and its epithelium, circulates in the capillaries. Thus there is an interchange of fluids, the result of which is the elaborated urine. The original objection to this theory, that an acid fluid is obtained by osmosis from an alkaline one, no longer holds, since laboratory experiment shows that such may actually take place.[1] On the other hand, if the tubules are stripped of their epithelium, as they often are in disease, urea is no longer eliminated so abundantly, although the conditions for osmosis remain even better than before.

In view of all the facts, the theory of Ludwig must be set aside and some such view as Bowman's adopted. But even here the "filtration" must be of a peculiar sort, and not wholly dependent on pressure; neither is it diffusion, but it probably partakes somewhat of the nature of an active process.[2] However this may be, under normal conditions the water and more diffusible salts, and

[1] *Vide* Tyson, Practical Examination of the Urine, 6th ed., p. 14.

[2] *Vide* Foster, Textbook of Physiology, 5th ed., p. 656 *et seq.*

under abnormal conditions such substances as albumen, sugar, and hæmoglobin, pass out through the glomeruli. Again, the epithelium has a two-fold activity, for it not only secretes some of the urinary constituents, e. g. hippuric acid and acid sodium phosphate, but it also has a selective function, — picking out of the blood, as it were, the products of retrograde metamorphosis, viz. urea and biliary pigments. There is also reason to believe that the epithelium shares in the production of water.

The separation of the urine is therefore a complex process, and no one theory can satisfactorily explain all the facts.

In the following pages frequent use will be made of the terms *relative* and *absolute amount;* they therefore require explanation at the outset. By the term "absolute amount" is meant the quantity that is actually excreted in twenty-four hours. It is generally used with reference to the solid constituents; but in performing the ordinary clinical tests, the amount of the solids will apparently vary according as they are dissolved in much or little water. This apparent proportion between the solids and the water is spoken of as the "relative amount."

# CHAPTER I.

## PHYSICAL CHARACTERISTICS OF THE URINE.

CONSISTENCY AND TRANSPARENCY.—Normal urine, when freshly passed, is a clear limpid fluid, dropping and flowing readily, like water.

Shortly after standing, there appears, somewhere between the top and bottom, a faint cloud made up of mucus and exfoliated epithelium derived from the genito-urinary tract. On longer standing, fermentative processes begin, the result of which is to render the urine, by the deposition of a sediment, more or less cloudy. The exact nature of this process will be considered further on.

The urine when freshly passed may be cloudy, especially if it be neutral or slightly alkaline, as, for instance, after a meal composed largely of vegetables or milk. This is owing to the separation of earthy phosphates; they gradually settle to the bottom, forming a somewhat bulky sediment. The addition of a few drops of acid will cause their immediate disappearance.

A temporary cloudiness is of no account; but if the urine is habitually turbid when passed, it indicates trouble. A transparent urine, however, is not necessarily normal.

Again, the urine may be perfectly clear when passed; but as its temperature falls, a deposit of mixed urates (K, Na, Ca, Mg) is not unlikely to occur. These salts, although soluble at the body temperature, are promptly precipitated in the cold, giving rise to a pinkish or reddish deposit characterized as "lateritious," or "brick-dust." The application of heat will cause the deposit, if it be of urates, to disappear; if of phosphates, to increase.

The urine of saccharine diabetes, although perfectly clear when passed, becomes turbid in a very short time. This is due to the growth of the sugar spore. In addition, a film covers the surface.

In tropical climates the urine is often cloudy, if not indeed decidedly milky, due to the presence of chyle. Ordinarily, sediments, on standing, settle to the bottom, leaving a clear supernatant fluid. Such is not the case with chylous urine: the cloudiness remains diffused through the fluid for many hours.

Finally, if the urine is alkaline, and contains pus, it may be viscid or "ropy."

If urine be shaken, a slight foam is developed on the surface, but it quickly disappears when

quiet is restored. It is said to be more permanent if the urine contain sugar or albumen. If the urine contain bile pigment, a permanent foam is developed, which is yellow or yellowish green in color.

AMOUNT. — Speaking broadly, the amount of urine passed may be taken as an index of the renal activity. On the average, the quantity for the twenty-four hours may be considered as not far from 1500 c.c. (40 to 50 oz.). This is, however, subject to considerable variation, not only between different individuals, but also in the same individual at different times. This variation depends on many conditions, viz. : —

*a.* There is a *diurnal variation* that is independent of other influences, — most being passed in the afternoon, less in the forenoon, and least during the night and early morning.

*b. Drink and Food.* — An excess of fluid taken into the system will cause a temporary increase in the flow of urine. Thus, a separation of 838 c.c. in an hour has been observed to follow the drinking of an excessive amount of water on an empty stomach. The ingestion of food has an influence upon the flow, for after meals there is an increase, whereas fasting will cause a diminution.

*c. Exercise.* — Prolonged exercise causes an increased activity of the sweat glands; and, bearing

in mind the complementary action between these glands and the kidneys, it follows that at the same time with the increased sweat production the flow of urine will be diminished. For the same reason, external cold, by decreasing the activity of the sweat glands, results in an increased flow of urine. Similarly, the reverse is true of external warmth. Hence it is that during the winter the flow of urine is on the average greater than it is in summer. All this indicates that a part of the renal function is concerned in preserving a normal aqueousness of the blood.

*d. Vaso-motor Action.* — Nerve filaments are distributed to the blood-vessels of the kidney. By disturbances in their function the flow may be increased, as in spastic polyuria, or diminished, as in suppression following a "catheter chill." Such disturbances are, in general, only temporary.

*e.* Finally, a diminished flow may be the result of *mechanical obstruction* somewhere in the urinary passages.

Pathologically, the amount varies a great deal. Certain diseases are characterized by a constant variation from the normal. In some, the flow is increased for a time, followed by a decrease; in others, the decrease is permanent from the beginning. In all cases of Bright's disease, there is a decided diminution at the close of life.

In acute stages of disease the amount is diminished. At the same time, the color as well as the specific gravity is high. As the acute stage passes over into the convalescent, the amount begins to increase, and even exceeds the normal, — more so in acute nephritis than in ordinary acute disease; but as convalescence becomes established, it falls to normal. In this way the turning or critical point may be approximately determined. Intermittent fever is, however, an exception, for the febrile character of the urine appears only on the *day after* the chill.

The amount is of greater importance in chronic than in acute disease.

In both forms of diabetes (mellitus and insipidus) the amount is greatly increased; viz. 3 to 6 litres in 24 hours. In chronic interstitial nephritis and amyloid degeneration of the kidney, the amount is increased; viz. 4 to 6 litres in 24 hours.

In chronic affections, combined with dropsy, the urine is much diminished, since the excess of water in the blood forms a constituent of the effusion. If absorption from the cellular tissues and serous cavities takes place, the amount of urine returns to the normal.

According to the amount of urine passed, three terms are employed, viz.: *Polyuria*, if the flow is

increased above the normal; *Oliguria*, if it be much less than normal; *Anuria*, or suppression, if no urine is passed. Each is to be regarded as a symptom, and not a disease.

Anuria, or suppression, may be due to either of two general classes of causes. *a.* Organic disease of the kidney or disturbances of innervation. *b.* Mechanical obstruction of any sort in the course of the excretory channels. Hence the former may be regarded as *non-obstructive* and the latter as *obstructive* suppression. These two classes vary in their course and symptoms. They will be again reverted to.

Specific Gravity (sp. gr.). — In health the specific gravity varies within tolerably wide limits. Inasmuch as it is a measure of the concentration of the urine, it will be influenced by all those conditions that alter the relation of the water to the solids; namely, drink, exercise, perspiration, the season (summer, winter), and nervous disturbances. The usual range of density, in health, may be put down as from 1018 to 1024, or, on the average, for mixed 24 hour urine, 1021. Pathologically, the variation is between 1003 and 1050.

In the acute febrile state, the amount of urine is diminished, while the urea, uric acid, and sulphates are absolutely increased. Consequently, in such cases the specific gravity ranges high. In

acute disease the appetite is greatly reduced, so that the increase of solids in the urine is probably at the expense of the permanent tissues; hence the wasting and emaciation of disease. As convalescence supervenes, the amount of urine increases beyond the normal, while the specific gravity falls below.

In chronic diseases, the total solids as well as the specific gravity fall below the normal. In general, chronic disease may be suspected when the amount, specific gravity, and total solids are just below normal. The two forms of diabetes are an exception. In both cases the total solids are largely in excess (125 to 150 grams), as well as the water; but in diabetes mellitus the sp. gr. is high, on account of the presence of a large amount of sugar, while in diabetes insipidus the sp. gr. is low, because the water is relatively increased. Hydruria resembles diabetes insipidus. The water is increased and the sp. gr. is low, but in hydruria the total solids are quite normal, or only slightly diminished. In chronic interstitial nephritis and amyloid degeneration the amount of water is large, but the sp. gr. is low, because the solids are diminished.

In general, during convalescence the specific gravity is below normal, the amount of water increased; while the solids are about normal.

In chronic parenchymatous nephritis and passive congestion, the amount of fluid is diminished, as well as the total solids, yet the specific gravity is high.

In a general way, the following deductions may be made: —

If the urine be diminished and the specific gravity high, it indicates, in health, either that little water has been ingested, or that free perspiration has taken place. Pathologically, it indicates the active stage of an acute or an exceptional chronic disease.

If the amount be large, and the specific gravity low, it indicates, in health, that excessive drinking has occurred. Pathologically, it suggests hydruria, diabetes insipidus, chronic interstitial nephritis, amyloid degeneration, and recovery from acute disease.

If the quantity as well as the specific gravity be low, it indicates a serious condition, which usually obtains just before death, and, in connection with kidney disease, betokens the dangers of uræmia. In some instances it indicates suppression, either obstructive or non-obstructive.

The specific gravity is most conveniently taken by means of the urinometer, various patterns of which, including the urinometer glass, are offered for sale. In general, those that have the olive-

shaped bulb or float, and read from 1000 to 1060, will be found most convenient for all practical purposes.

If, in determining the specific gravity the quantity of urine be too little to fill the urinometer glass, it may be diluted with distilled water sufficiently to fill the glass to the required height. From the specific gravity of this mixture that of the urine can be calculated. E. g. suppose that four volumes of water are added to one of urine, making five volumes in all, and that the specific gravity of the mixture is 1004, then that of the urine will be $1000 + (4 \times 5) = 1020$. In such calculations the reading of the urinometer must be as accurate as possible, lest the error of reading be also multiplied by the number of volumes.

Solids. — Under normal conditions the total solids amount to about 72 grams in 24 hours. As a rule, females eliminate less and children more per kilogram of weight than males.

An estimation of the total solids is of great value, inasmuch as they indicate (*a*) the rapidity of the vital processes, and (*b*) the capacity of the kidney for work. To make such knowledge of value, it is important to know the amount of urine passed, and also at what time or during what periods of time it is passed.

The solids may be roughly estimated from the specific gravity by multiplying the last two figures by $2\frac{1}{3}$ for each litre of urine. E. g. quantity of urine passed in 24 hours, 1500 c.c.; sp. gr. 1021. Then $21 \times 2\frac{1}{3} = 49$ for 1 litre, or 1000 c.c.; for 1500 c.c., or $1\frac{1}{2}$ litres, $49 \times 1\frac{1}{2} = 73\frac{1}{2}$, which represents the amount in grams of the total solids in the above specimen.

Color. — The color of urine in health is a light yellow or amber, but varies in intensity from the palest straw to a full amber or red. A dark urine is abnormal.

The most usual variations of color are due either to dilution, i. e. anything that causes a relative increase in the water; or to concentration, i. e. any cause for a relative decrease of the water. Such causes have been studied in the preceding paragraphs. In fever there is an actual increase of metabolic processes, and consequently an absolute increase of color pigment. Hence fever urines are high-colored. Some maintain that the peculiar high color of fever urines is due to an abnormal pigment, uroerythrine.

It is therefore common to classify the color of urine as pale, normal, high, or dark.

A dark color always means the presence of an abnormal coloring matter. Usually it is some shade of brown or green, and in most cases is due

to blood or bile. Bile pigment may give rise to either a brown or green hue. If the color be due to bile, on shaking the urine in a test tube a permanent greenish-yellow foam is developed.

Rarely, the color may be a dirty blue. In such instances, there is a similarly colored sediment, and upon the surface a dark blue film. The urine is usually alkaline, and chiefly found associated with cholera and typhus fever. The pigmentation is due to indigo, through the decomposition of indoxyl.

Finally, the color may be influenced through the absorption by the system of various substances. E. g. creosote, tar ointment, carbolic, gallic, and salicylic acids may give rise to dark urines. Rhubarb and santonin impart a yellow shade to the acid urine, which on the addition of an alkali turns to red. Senna communicates a brownish, and logwood a reddish tinge to the urine.

Odor. — In general, the odor is characteristic, and is spoken of as "urinous." It is of no consequence unless ammoniacal. Certain drugs (turpentine, copaiba, cubebs, oil of sandal-wood) and certain articles of food (asparagus, garlic) communicate peculiar and characteristic odors to the urine. Diabetic urine, when fresh, has an odor of new-mown hay. Turpentine imparts to the urine the odor of violets.

REACTION. — The reaction of the mixed twenty-four hour urine is always acid, and is equivalent to from 2 to 4 grams of oxalic acid. The acidity is probably due to the acid sodium phosphate ($NaH_2PO_4$), assisted perhaps by other acid constituents, such as uric and hippuric acids, and, under some circumstances, by a few of the fatty acids, e. g. acetic and lactic.

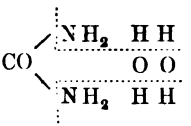
Phosphoric acid is tribasic ($H_3PO_4$), and hydrogen can be replaced by either one, two, or three equivalents of sodium; namely, $Na_3PO_4$, alkaline; $Na_2HPO_4$, neutral, or slightly alkaline; $NaH_2PO_4$, acid. The neutral phosphate, $Na_2HPO_4$, is a constituent of the blood. The dibasic uric acid ($H_2\bar{U}$) is also present in the blood, and between them a mutual exchange of H for Na occurs, viz. : —

$$Na_2HPO_4 + H_2\bar{U} = NaH\bar{U} + NaH_2PO_4.$$

The acid sodium phosphate passes by osmosis through animal membranes, whereas the neutral salt does not. Hence it is that the kidneys separate the former, and not the latter.

The acidity of the urine may be neutralized by any compound of ammonium, such as urea. By organic decomposition, urea takes up one molecule of water, giving two molecules of ammonia, and one molecule of $CO_2$. These readily recom-

bine with one more molecule of water to form one molecule of ammonic carbonate, $(NH_4)_2CO_3$. This reaction goes on in all urines on standing, and it may be hastened in the fresh by the addition of a little stale urine, as that of an old cystitis.




Pasteur showed that urea was changed into carbonate of ammonium by the action of a micrococcus (M. Ureæ), and it is now pretty well established that the production of ammoniacal urine is a kind of bacterial fermentation. The fact that stale urine hastens the change is explained on the ground that it is highly charged with bacteria of all kinds, including the M. Ureæ.

Another view of the alkaline fermentation is based on the destructibility of urea by a peculiar ferment discovered by Musculus; he recommends a paper saturated with this ferment as a very sensitive test-paper for urea. The alkaline urine of cystitis is filtered; the filter-paper is washed with distilled water until it no longer has an alkaline reaction. It is then dried and colored with turmeric. Urea itself does not react on turmeric, but the urea is decomposed to ammonium carbonate by the absorbed ferment, and the paper is therefore colored brown.

If the urine is ammoniacal *when passed*, it nearly always indicates a cystitis or pyelo-cystitis.

The alkalinity, however, may be due to a fixed alkali (Na or K) circulating in the blood. In case of doubt the *vapor* of the heated urine may be tested with turmeric paper. If the test responds the alkali must be volatile ($NH_4$).

When the blood is excessively alkaline, as after a meal composed largely of vegetables or milk, it modifies the acidity of the urine, and in fact may for a short time render it slightly alkaline.

Urine may be excessively acid from concentration, as is the case in fevers.

A highly acid urine favors the deposition of oxalate of calcium and uric acid crystals. If separation occurs within the urinary passages, a local irritation is set up, which may lead to more or less serious inflammation, as well as to the formation of calculi.

After standing awhile at a moderate temperature, the acidity of the urine increases; the color becomes high, and the normal mucous cloud, increased by the separation of the acid urates and uric acid, finally settles to the bottom. This is called the stage of acid fermentation. After longer standing, though quite rapidly in hot weather, the reaction changes to alkaline, the color becomes paler, and, owing to the deposition

of many substances to be studied hereafter, the turbidity increases. This change constitutes the stage of alkaline fermentation.

Fresh urine, hermetically sealed in an aseptic vessel, will remain fresh for years.

## CHAPTER II.

### CHEMICAL CHARACTERISTICS.

THE constituents of the urine are numerous, and, although subject to wide variations, even in health, yet the following table may be taken as showing the average amounts eliminated in the twenty-four hours.

URINARY CONSTITUENTS PASSED IN TWENTY-FOUR HOURS. (AFTER PARKES.)

| | By an average mass of 66 kilos (145 lbs.). | Per 1 kilo of body weight. |
|---|---|---|
| | Grams. | |
| Water | 1500.000 | 23.0000 |
| Total solids | 72.000 | 1.1000 |
| Urea | 33.180 | .5000 |
| Uric acid | 0.555 | .0084 |
| Hippuric acid | 0.400 | .0060 |
| Kreatinin | 0.910 | .0140 |
| Pigment and other substances | 10 000 | .1510 |
| Sulphuric acid | 2.012 | .0305 |
| Phosphoric acid | 3.164 | .0480 |
| Chlorine | 7.000 | .1260 |
| | (8.21) | |
| Ammonia | 0.770 | |
| Potassium | 2.500 | |
| Sodium | 11.090 | |
| Calcium | 0.260 | |
| Magnesium | 0.207 | |

It will be seen that urea and chlorides are the principal constituents, and, the others remaining unchanged, any marked increase or decrease in the excretion especially of urea or of chlorides will notably influence the specific gravity of the urine. The same is true to a lesser degree of the other solids.

### Normal Organic Constituents.

Urea ($\dot{\bar{U}}$) is the most important solid constituent of the urine. It is the final product of the retrograde (oxidative) metamorphoses of the nitrogenous tissues. As such, it is formed throughout the body and taken up by the circulating blood, from which it is separated by the functional activity of the kidneys. When for any reason the kidneys become incapable of eliminating urea, the sweat glands to a certain extent assume their lost or impaired function, and urea is then detected in the sweat.

Urea, however, is not formed from the albuminoid tissues direct, but it has been found that many intermediate stages, with their corresponding products, exist. Among the latter are uric acid, leucine, and tyrosine. When, for example, the oxidative processes are seriously impaired (e. g. acute yellow atrophy of the liver and typhus fever), no urea is found in the urine, but in its

place leucine and tyrosine; furthermore, if these substances are ingested by a healthy individual, his nitrogenous excreta ($\dot{U}$) is found to be increased by just so much nitrogen as was contained in the amount of leucine and tyrosine taken into the system.

The average amount of urea passed in twenty-four hours is from thirty to forty grams, with a normal variation of one fifth below or above this amount. Women and children excrete less urea than men, but children more, in proportion to their body weight. A normal urine may be said to contain $2\frac{1}{2}\%$ of urea.

Urea can be made artificially in many ways, and most readily from ammonium cyanate. It is a white (somewhat brownish when made from urine) crystalline solid, freely soluble in water and alcohol, but insoluble in ether. By the addition of nitric acid, nitrate of urea is formed. Under the microscope the nitrate crystals appear singly, or in overlapping layers, as rhombic or hexagonal plates.

*Tests for Urea.* — The clinical method of testing for urea is to add a drop or two of nitric acid to a like quantity of urine in a watch crystal. If the amount of urea present is normal, in from twenty to thirty minutes delicate crystals of nitrate of urea appear in the fluid. A very warm room or

an excess of urea will hasten the crystallization, and *vice versa*. This is only an approximate test, and if the acid is impure (contains $HNO_2$) it decomposes the urea, thus:

$$CH_4N_2O + HNO_3 + HNO_2 = NH_4NO_3 + H_2O + CO_2 + N_2.$$

The mixture should never be warmed, as it facilitates the decomposition. In cases where the urea has already decomposed (cystitis), this test cannot of course be applied.

As it is often of importance to know the precise quantity of urea excreted, many quantitative tests have been devised; but of these the following, based on the fact that a chlorinated compound acting upon urea gives rise to a single gas, is the most popular, viz.:

$$CH_4N_2O + 3\,NaOCl = 3\,NaCl + 2\,H_2O + CO_2 + N_2.$$

The same reaction occurs with either calcic hypochlorite or sodic hypobromite.

The apparatus for performing the test consists essentially of two parts. 1. A burette graduated to 60 c.c., as indicated in the figure. 2. A double-bulbed flask, each bulb of 100 c.c. capacity, and united as indicated in the figure. The burette, fastened by a clamp to a retort stand, is immersed in a large beaker of water, so that the fluid inside of the burette stands at the zero line; or the

burette may be similarly, but tightly, adjusted to a perforation in a cork which fits the mouth of the

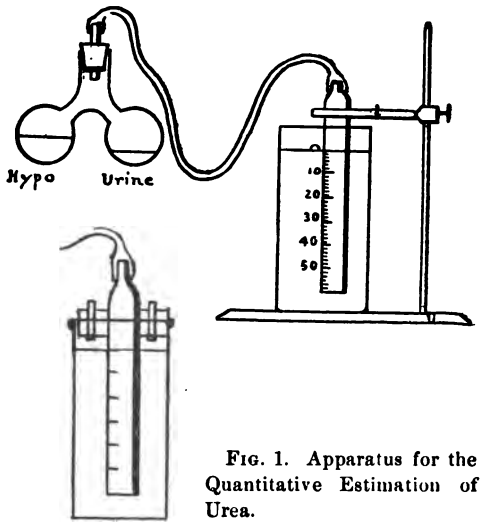



FIG. 1. Apparatus for the Quantitative Estimation of Urea.

beaker. A few perforations of the cork outside the burette are necessary in order that air may escape from the beaker when the apparatus is put in operation. The flask, with a tightly fitting cork through which a bit of glass tube is passed, is then connected with the burette by rubber tubing.

To perform the test, 5 c.c. ($2\frac{1}{2}$ c.c. if high colored and concentrated) of urine are poured into one of the bulbs, while a sufficient amount of calcic hypochlorite is placed in the other. Having con-

nected the two parts of the apparatus as indicated in the figure, the double-bulbed flask is so agitated as to allow thorough commingling of the urine with the hypochlorite. Effervescence at once commences, and the liberated nitrogen gas passes over into the burette and drives out the fluid. When effervescence has ceased the amount of water displaced by the gas is read off, and from that the quantity of urea is calculated, — based on the fact that at 0° C. and 760 mm. barometer, 1 gram urea = 370 c.c. N. For example: if, when the reaction has run to an end, 40 c.c. of nitrogen are recorded on the burette, in accordance with the assumption that 1 gram of urea = 370 c.c. N, the following proportion can be made:

$$370 : 40 = 1 : x \ (= .108+).$$

This represents the amount of urea (in grams) in 5 c.c. of urine (the quantity used in the experiment). Obviously, in 1500 c.c. urine (assuming that to be the amount passed in 24 hours) there must be $(.108 \times \frac{1500}{5} =)$ 32.4 grams.

In all tests for urea, save the above, albumen must first be removed.

To avoid the necessity of calculation, the following table has been arranged, from which at a glance, the cubic centimeters of nitrogen having been determined, the amount of urea can be estimated.

## TABLE FOR UREA IN URINE.

For 15–20° C. 63–69° Fahr. Using 5 c.c. Urine.

| C. C. Nitrogen. | Urea per Litre in Grams. | Urea per Ounce in Grains. | C C Nitrogen. | Urea per Litre in Grams. | Urea per Ounce in Grains. |
|---|---|---|---|---|---|
| 20 | 10.24 | 4.75 | 36 | 18.44 | 8.86 |
| | 10.50 | 5.06 | | 18.70 | 9.00 |
| 21 | 10.76 | 5.15 | 37 | 18.96 | 9.09 |
| | 11.01 | 5.30 | | 19.21 | 9.25 |
| 22 | 11.27 | 5.39 | 38 | 19.47 | 9.34 |
| | 11.52 | 5.54 | | 19.73 | 9.48 |
| 23 | 11.78 | 5.62 | 39 | 19.98 | 9.58 |
| | 12.04 | 5.78 | | 20.24 | 9.73 |
| 24 | 12.29 | 5.87 | 40 | 20.49 | 9.82 |
| | 12.50 | 6.01 | | 20.75 | 9.96 |
| 25 | 12.81 | 6.17 | 41 | 21.00 | 10.12 |
| | 13.06 | 6.26 | | 21.26 | 10.21 |
| 26 | 13.32 | 6.40 | 42 | 21.52 | 10.35 |
| | 13.58 | 6.49 | | 21.77 | 10.44 |
| 27 | 13.83 | 6.65 | 43 | 22.03 | 10.60 |
| | 14.09 | 6.74 | | 22.28 | 10.69 |
| 28 | 14.35 | 6.88 | 44 | 22.54 | 10.83 |
| | 14.60 | 7.03 | | 22.80 | 10.99 |
| 29 | 14.86 | 7.13 | 45 | 23.05 | 11.08 |
| | 15.11 | 7.27 | | 23.31 | 11.23 |
| 30 | 15.36 | 7.36 | 46 | 23.57 | 11.31 |
| | 15.62 | 7.51 | | 23.82 | 11.47 |
| 31 | 15.87 | 7.61 | 47 | 24.08 | 11.56 |
| | 16.13 | 7.75 | | 24.34 | 11.70 |
| 32 | 16.39 | 7.84 | 48 | 24.59 | 11.79 |
| | 16.65 | 7.99 | | 24.85 | 11.95 |
| 33 | 16.91 | 8.13 | 49 | 25.10 | 12.09 |
| | 17.16 | 8.23 | | 25.36 | 12.18 |
| 34 | 17.42 | 8.38 | 50 | 25.62 | 12.28 |
| | 17.67 | 8.47 | | | |
| 35 | 17.92 | 8.62 | | | |
| | 18.18 | 8.71 | | | |

*Causes of Variation in the Amount of Urea.*— In general, urea is increased whenever the supply of nitrogen to the body or the body metabolism itself is increased. Such causes may be stated in tabular form, thus:—

UREA.

| Increase. | Diminution. |
|---|---|
| Nitrogenous diet. | Vegetable diet. |
| Ingestion of compounds of ammonium. | Chronic diseases in general. |
| Excessive mental or physical exercise. | Dropsical conditions.[2] |
| Nervous disturbances. | Liver diseases.[3] |
| Excessive drinking. | |
| Active stage of acute disease.[1] | Recovery from acute disease (nitrogen going to repair the wasted tissues). |
| Gout. | |
| Diabetes mellitus.[4] | Onset of death. |
| Diabetes insipidus (especially).[4] | |

## Substances allied to Urea.

*Kreatin* is a normal constituent of muscle tissue, but not of the urine. It is intimately related to

[1] Intermittent fever an exception. Urea is increased in the interval between the paroxysms. *Vide* p. 11.

[2] In dropsical conditions the urea passes into the effusion, and as this is reabsorbed, the urea increases.

[3] In disease of the liver, the urea bears a direct proportion to the working capacity of this organ. In acute yellow atrophy the urea is diminished, because it is eliminated prematurely as leucine and tyrosine.

[4] An exception to the rule for chronic diseases. *Vide* p. 13.

*Kreatinin*, which is a normal constituent of the urine. By the addition of a single molecule of water, kreatinin becomes kreatin. Kreatinin is found in the urine only after the ingestion of animal foods has begun.

*Sarkine*, *Xanthine*, and *Uric Acid* are intermediate products of oxidation on their way to urea. Sarkine has no clinical importance. Xanthine, combined with uric acid, may form a constituent of urinary calculi. It is also present in the lungs and spleen. If xanthine and nitric acid be evaporated to dryness, and potassic hydrate added thereto, a pinkish color changing to purplish blue is developed, — so-called murexide test.

URIC ACID ($\bar{U}$) is present, normally, in small amount, — $\frac{1}{2}$ gram in twenty-four hours. It may be increased to four grams; but such an increase is due to abnormal conditions of the system, and is independent of dietary influences.

Uric acid is a more complex substance than urea; one molecule of uric acid splitting up, under certain circumstances, into two molecules of urea and a compound of oxalic acid. In the urine of the carnivora, e. g. birds and reptiles, uric acid replaces urea as the chief nitrogenous excretion. It is a weak dibasic acid, and occurs in human urine, not as a free acid, but combined with the alkaline bases sodium and potassium, and to a less extent with calcium and ammonium.

The metabolic changes in the albuminoid tissues result in the formation of uric acid ($H_2\bar{U}$). In the blood it meets the alkaline sodic phosphate, and the following reactions occur:

$$Na_2HPO_4 + H_2\bar{U} = NaH_2PO_4 + HNa\bar{U};$$
$$Na_2HPO_4 + HNa\bar{U} = NaH_2PO_4 + Na_2\bar{U}.$$

The products of the second reaction pass with ease through animal membranes, and therefore appear in the urine.

By oxidation uric acid passes into urea. There are, however, intermediate steps, in which alloxan and parabamic, oxaluric, and oxalic acids are formed.

If nitric acid be added to uric acid, alloxan and urea are formed. The reduction of alloxan gives alloxantin. Ammonium hydrate, when added to a mixture of alloxan and alloxantin, gives murexide. The murexide reaction forms the chief test for uric acid. A similar reaction, however, is obtained from xanthin with potassic hydrate. If heat be applied, the color if due to uric acid promptly disappears, whereas if due to xanthin it increases in intensity.

In alkaline solution uric acid is a powerful reducer. If paper moistened with silver nitrate be dipped in an alkaline solution of uric acid, metallic silver is deposited on the paper. This reduc-

tion is even more marked with solutions of copper. (Compare Trommer's test for sugar.)

*Tests.* — If a little hydrochloric acid be added to a test-tube half filled with urine, in the course of twenty-four hours crystals of uric acid will be found on the sides and bottom of the tube. A sufficient and quicker clinical test will be mentioned under Tests for Albumen.

*Variation in the Amount of Uric Acid.* — It is sufficiently evident, inasmuch as urea represents the final product of complete oxidation and uric acid only one of the intermediate stages, that any cause whereby oxidation is hindered will give rise to an increased elimination of uric acid. Such is found to be the case especially in pneumonia ($1\frac{1}{2}$–2 grams in 24 hours); also in pulmonary tuberculosis, chronic gout, acute rheumatism, and lung and heart diseases accompanied by dyspnœa and indigestion. Under conditions of health, when the amount of urine is diminished, the uric acid may be relatively increased.

Uric acid forms two classes of salts, the neutral and the acid. The former are readily soluble in water, the latter considerably less soluble, whereas uric acid itself is almost insoluble, although, like the acid salt, more soluble in hot than in cold water. If for any reason there exists in the economy a diminished supply of bases or an

over supply of uric acid, the latter will fall out of solution and appear as a sediment in the urine. Such a separation occurring in the course of the urinary passages gives rise to "gravel," which in turn may act as the starting point of "stone or calculi."

HIPPURIC ACID forms only a small constituent of human urine, but in the urine of the herbivora it occurs in large quantities, and appears to supply the place of uric acid. It is derived more or less directly from the constituents of the food containing substances belonging to the aromatic series (benzoic acid or its radical). The benzoic acid meets glycocoll, a constituent of the body, and hippuric acid is formed. There is reason to believe that this change is in part accomplished through the activity of the renal epithelium.

It is detected by the same test as that employed for uric acid, but hippuric acid is soluble in hot alcohol, whereas uric acid is not. Hippuric acid does not respond to the murexide test.

*Variation in the Amount of Hippuric Acid.* — It is increased by a diet of vegetables or substances containing the benzoic acid radical, e. g. such fruits as greengages and whortleberries. Hippuric acid is also increased in diabetes, in which disease it more or less replaces uric acid. Finally, if ten grains of benzoic acid be taken at night, in the

morning crystals of hippuric acid will be found in the urine.

PHENOL (*phenylic acid*, *carbolic acid*) is never found *as such* in normal urine, but as a salt of phenol-sulphuric acid. It is to this substance, of which 15–20 mg. are eliminated in the twenty-four hours, that the pleasant odor of fresh urine is mainly due.

Among the products of intestinal fermentation are *phenol*, *indol*, and *skatol*, of which phenol is found in the intestine between the other two, i. e. indol being formed higher up, while skatol is formed lower down in the intestine. The conditions, therefore, that give rise to phenol and indol are identical, except that indol is formed earlier in point of time. A portion of the phenol may be obtained from the fæces, while the rest finds its way into the urine.

After absorption into the system, phenol as such disappears, for it meets sulphuric acid, and phenol-sulphuric acid, which is not poisonous, is formed. [The proper antidote for carbolic acid poisoning, then, is an alkaline sulphate with which the phenol may combine to form the phenol-sulphuric acid.]

When present in excess, phenol imparts to the urine a dark color, which *may* not appear until after the urine has left the body and stood a while. If the presence of phenol in the system is suspected,

it is an important step to test the urine for the sulphates. If phenol is present, the sulphates will of course be absent.

The test for phenol: when boiled with a solution of calcic hypochlorite, phenol imparts a green color to the solution.

In peritonitis and septic diseases, the phenol of the urine is increased. Under the same conditions, indoxyl is also increased. In fact, they follow each other very closely.

The COLORING MATTERS of the urine are normally two: *urobilin* and *indoxyl.*

UROBILIN (hydrobilirubin, urohæmatin, UROPHÆIN) is derived more or less directly from the blood. The decomposition in the liver of the hæmoglobin of the blood gives rise to bilirubin, which, as a constituent of the bile, passes into the intestine. Here it is reduced by the action of water and nascent hydrogen (hydrogen is a product of intestinal fermentation and represents 50% of the total gases), and urobilin is formed. This is then absorbed and excreted by the kidneys. Thus, the direct descent of urobilin from the blood is established. It would appear, then, that the amount of urobilin in the urine might be taken as a measure of the decomposition of the blood, and such appears to be the case; for diseases in which there is an increased destruction of the blood

globules are characterized by an increase both in the bile pigment and the urobilin of the urine. Jaundiced urines contain, besides free bile pigment, an increased amount of urobilin.

Urobilin in concentrated alkaline solution possesses a dark brown color, and in dilute solutions a rose-red or pinkish hue. For practical purposes the color is graded to a system of units, of which 15 corresponds to that normally found in the urine. In acute disease (typhoid and typhus fevers) the color may rise as high as 60.

Urobilin is set free by sulphuric acid, and upon this fact is based *Heller's test for urophæin.* About 2 c.c. of colorless sulphuric acid is poured into a collamore wine-glass, and into it, from a height of four or five inches, twice as much urine is allowed to fall. The urine mingles intimately with the acid, and if the amount of urophæin is normal a deep garnet-red color is at once developed. If the urophæin is increased, the color developed is black and opaque; if diminished, it is paler, wine-red, and more or less transparent. It should be remembered that urine containing sugar, blood, or bile pigments gives an apparent increase of urophæin. It is also curious to note that the ingestion of potassic chlorate causes a diminution of the color reaction.

Uroxanthin was the name given by Heller to

the well known substance *indican* (of the Indigo group). It has now been found that, as a coloring matter of the urine it is not *indican*, but *indoxyl* (an oxidized product of indol), and that it exists in the urine as a sulphate. It is not, properly speaking, a urinary pigment, but under certain conditions it may be decomposed with the liberation of indigo, the latter imparting to the urine a blue or violet color. This decomposition may occur high up in the urinary passages, and so give rise to the dirty blue urine previously alluded to (page 17).

In the course of pancreatic digestion, or as a result of intestinal fermentation, indol is formed. This is absorbed into the blood where by oxidation (one atom of O) it is changed to indoxyl. It then pairs off with sulphuric acid to form indoxyl-sulphuric acid, and subsequently indoxyl sulphate of potassium. The last, when heated out of contact with the air, splits into potassic sulphate and sulphuric acid. When oxidized, it changes to the acid sulphate of potassium and indigo-blue; under certain conditions, to indigo-red. Skatol is formed late in the digestive processes, and is found in the fæces. It is believed that skatol contributes to the formation of indigo-red, but how is not at present known. At all events, skatol is quite analogous to indol, and between the two an intimate chemical relation exists.

*Heller's test* is performed as follows: 4 c.c. of pure hydrochloric acid are poured into a collamore wine-glass, and to it are added about 20 drops of urine. The mixture is stirred, and, if the amount of indoxyl present be normal, a delicate amethystine color is developed. The test is rendered more delicate if 2 or 3 drops of nitric acid are added first. If iodide of potassium has been ingested, the addition of the $HNO_3$ is unnecessary, as iodine, which is itself a powerful oxidizer, is liberated. According as the amount of indoxyl present is more or less than normal, so will the intensity of the color vary.

*Variation in the Amount of Indoxyl.* — A decrease of indoxyl is not pathological. It simply indicates a dilute urine. Indoxyl is increased in those conditions in which intestinal digestion is so interfered with as to cause an increased formation of indol. Normally the urine of twenty-four hours contains 5–20 milligrams of indoxyl. This may be increased, notably in peritonitis, to 100 mg. There is also a large increase in cholera. Furthermore, indoxyl is increased in simple fever, obstructive disease of the *small* intestine, chronic diseases, such as malignant disease of stomach or liver, rickets, pulmonary consumption, amyloid degeneration of kidney (if associated with consumption), chronic interstitial nephritis, Addison's disease,

phenol poisoning, septic diseases, and diseases in which nerve tissue is being destroyed. It is also increased by an exclusively meat diet, after coitus, and following the ingestion of indol. Grossich declares that in every case of fracture, or other bone lesion, the urine contains an excess of *indican*, and suggests that in doubtful cases it should be looked for. Finally, there may be a relative increase due to concentration of the urine, e. g. in hot weather.

With increased indoxyl, there is always an associated increase of phenol.

### Normal Inorganic Constituents.

The inorganic salts exist in the urine, for the most part, in natural solution, the composition of the ash corresponding very closely to the results of direct analysis. The ash for 24 hours is from 10 to 20 grams. The chief bases are sodium, potassium, calcium, and magnesium. There are traces of iron and silicon. These appear to be combined, for the most part, with hydrochloric, phosphoric, sulphuric, uric, and hippuric acids.

Chlorides (Cl). — Chlorine combined with sodium to form sodium chloride is the most abundant inorganic constituent of the urine. There are also small quantities of potassium and ammonium chloride present, but the amount is so insignificant

that they may all be considered together. In health, the chlorides of the urine correspond almost exactly with the amount taken in with the food. The quantity recovered from the urine in 24 hours is not far from 10 to 12 grams.

*Tests.*—Heller's clinical test is based on the fact that a solution of nitrate of silver throws down, in *acid* solution, the chloride of silver. A collamore wine-glass is half filled with urine. A few drops of nitric acid are added (otherwise the addition of the silver nitrate is liable to precipitate the phosphates as well as the chlorides) to render it acid; then from a pipette or dropper is allowed to fall a single drop of the silver nitrate solution (1 part to 8). As a result, if the quantity of chlorides is *not* diminished, chloride of silver in the form of a white cheesy lump is at once formed in the urine. If the chlorides are slightly diminished, then the cheesy lump which forms slowly disintegrates, giving the urine a more or less milky look. If they are diminished to $\frac{1}{10}$ of 1% or less, a simple cloudiness follows the addition of the $AgNO_3$. Finally, should no precipitate occur, the chlorides are probably absent.

The *quantitative test* is a volumetric one, devised by Mohr. There are required: —

1. Cold saturated solution of neutral chromate of potassium.

2. A solution of silver nitrate, such that 1 c.c. = 10 mg. NaCl. [Dissolve 29.075 grams pure fused silver nitrate in distilled water, and dilute to a litre.]

*Process.*— Ten c.c. of urine are put into a platinum crucible, and two grams of potassium nitrate (free of chlorides) added. The mixture is slowly evaporated over the water-bath to dryness. The residue is heated, at first gently, then intensely, until the carbon is completely oxidized (residue white). The crucible is then placed in a beaker of water to dissolve the slag. When this is dissolved, the crucible is removed, and washed off with a wash-bottle, care being taken that the wash water flows into the "slag solution." The solution is then made slightly acid by dilute nitric acid (free of chlorine) and again neutralized by a pinch of calcium carbonate. To this mixture, without regard to the sediment, two or three drops of the potassium chromate solution are added, and the silver solution allowed to run in from the burette until a distinct red color remains. [The silver combines preferably with chlorine. When, however, all the chlorine has been consumed, it unites with the chromic acid radical to form chromate of silver. This, being red, colors the fluid, and indicates the point at which all the chlorine present has united with the silver.] The

amount of silver nitrate solution used is then read off from the burette, and the quantity of chloride calculated as follows. Suppose exactly 8 c.c. of the silver solution were used. Since 1 c.c. $AgNO_3$ solution = .010 gram chloride (or 10 mg.), 8 c.c. = .080 gram; and since 10 c.c. of urine (the amount used in the test) contain .080 gram, 1500 c.c. (or the amount passed in 24 hours) contain $.080 \times \frac{1500}{10}$, or 12 grams.

*Variation in the Quantity of Chlorides.* — There is no pathological increase of chlorides. They are diminished in all acute febrile conditions, especially if there is an exudation of which they form a part. As soon as the exudation ceases and absorption begins, they increase, or, if absent, reappear in the urine. It may therefore become at times a matter of some clinical importance to test the urine for chlorides, e.g. in acute pneumonia. In this disease the chlorides may wholly disappear from the urine after the third or fourth day. Their reappearance would then indicate the critical or turning point of the disease.

In all other acute febrile diseases accompanied by serous exudation or watery diarrhœa, — pleurisy, peritonitis, meningitis, acute rheumatism, pyæmia, and septicæmia, — or chronic diseases accompanied by dropsy, the chlorides are diminished. As an aid in differentiating typhoid fever from

meningitis, it may be said that the chlorides disappear from the urine with greater rapidity in the latter disease.

PHOSPHATES. — The phosphoric acid of the urine is divided between the alkalies (Na and K) and alkaline earths (Ca and Mg) forming the so-called alkaline and earthy phosphates. The amount of phosphoric acid excreted in the 24 hours is from 3 to $3\frac{1}{2}$ grams, of which two thirds are in combination with the alkalies.

*The Earthy Phosphates* (E. P.), namely, calcium and magnesium, constitute only a small proportion of the total phosphates. Of this proportion about two thirds is magnesium, and one third is calcium phosphate. Both are present as the acid salt, — $CaHPO_4$ and $MgHPO_4$; and both are soluble in acids, but insoluble (the Mg salt, however, is slightly soluble) in water.

In nearly neutral urines, boiling decomposes the phosphates, viz. :

$$\underset{\text{(Heated.)}}{4\,CaHPO_4} = \underset{\text{(Soluble in alkaline solution)}}{Ca_3(PO_4)_2 + CaH_4(PO_4)_2}$$

Lest the precipitate thus formed should be mistaken for albumen, it is customary in the heat test for this substance to add a few drops of acetic acid to keep the phosphates in solution.

*Detection.* — To a test tube half filled with clear

(filtered) urine, a few drops of ammonic hydrate are added. Upon warming the mixture, the earthy phosphates separate out and in 10 or 15 minutes settle to the bottom of the tube. If the deposit thus formed is from $\frac{1}{4}$ to $\frac{1}{2}$ an inch deep, the amount may be said to be within normal limits.

In normal urine the earthy phosphates are precipitated *white*, but if the urine contains an abnormal pigment, — blood, bile, or vegetable coloring matter, — they carry down the pigment with them, and so may be variously colored. *Vide* Color of Urine, p. 16.

*The Alkaline Phosphates* (A. P.), viz. sodium and potassium, are present almost wholly as acid salts. They are soluble in water, and, unlike the earthy phosphates, are not precipitated by alkalies. The acidity of the urine is due in large measure to the acid sodium phosphate.

*Detection.* — To the filtrate (in another test tube) of the earthy phosphates, about one third as much of the magnesian fluid (saturated solution $MgSO_4 + NH_4Cl$) is added. A white precipitate of the alkaline phosphates occurs, which settles to the bottom of the tube. If the precipitate is from $\frac{1}{2}$ to $\frac{3}{4}$ inch deep, the quantity is normal.

*Qualitative Test, — volumetric process.* — The solutions required are: —

1. Sodium acetate solution. 100 grm. $Na\bar{A}$ are

dissolved in 900 c.c. of water, and 100 c.c. acetic acid added.

2. Nitrate of uranium solution, so made that 1 c.c. corresponds to 5 milligrams of phosphoric acid.

3. Solution of potassic ferrocyanide.

*Process.* — 50 c.c. of urine and 5 c.c. of the sodium acetate are warmed together over the water bath. To this the uranium solution is added drop by drop as long as a precipitate is observed, or until a drop of the urine mixture, when brought into contact with a piece of filter paper wet with the ferrocyanide, develops a brown color. The number of c.c. used (uranium solution) multiplied by 0.005 will give the quantity of phosphoric acid in 50 c.c. of urine. From this the amount contained in the twenty-four-hour urine is readily calculated.

*Variations in Quantity of Phosphoric Acid.* — (The inferences are drawn from the acid alone.)

Bony and nervous tissues contain phosphorus, and their destruction by disease will be accompanied by an increase in the phosphates of the urine. Lung tissue also contains phosphorus, and in the early stages of phthisis the phosphates of the urine are increased. An increase is also noticeable in polyuria, and especially after the ingestion of phosphatic food or salts of phosphorus. A diurnal

variation of the phosphates, corresponding closely to the normal daily variation alluded to in connection with the quantity of the urine, is said to exist.

A persistent excess of phosphates in the urine is termed *phosphaturia.* Inasmuch as this condition, in which the amount of phosphates may reach as high as 7 to 10 grams in the 24 hours, gives rise to symptoms not unlike those of saccharine diabetes, it was formerly called *phosphatic diabetes.* With phosphaturia, glycosuria may or may not coexist. In case such a combination exists, an increase of sugar is accompanied by a decrease of the phosphates, and *vice versa.*

SULPHATES (Sf). — These appear in the urine as the result of the oxidation of sulphur compounds (albumens contain S), chiefly in the form of the neutral sulphates of sodium and potassium. The normal daily excretion lies between 2 and 4 grams. Any sulphate taken into the body is completely eliminated in from 18 to 20 hours.

*Test.* — To $\frac{1}{2}$ a test tube of urine, one third as much of the barium solution (saturated solution $BaCl_2 + \frac{1}{8}$ HCl) is added. A white precipitate falls, which, if it fills one half the concavity of the test tube, may be considered normal in amount.

*Variation in the Quantity of Sulphates.* — The ingestion of sulphur, or any salt or fluid (mineral

waters) containing it, will be followed by an increase of the sulphates in the urine. They are also slightly increased, following the urea very closely, whenever the metabolic processes are increased.

The sulphates are diminished whenever there is a poor appetite, when phenol has been absorbed into the system, or when any substance is present that will unite to form a sulpho-acid.

In the ordinary clinical analysis of the urine, it is not important to test for the presence of the sulphates, except when poisoning by phenol is suspected. (*Vide* Phenol, p. 34.)

### Abnormal Constituents.

The abnormal constituents of the urine consist chiefly of albuminous, saccharine, and coloring matters. In addition to these, various other substances, representing either the products of impaired metabolism or the elimination unchanged of many mineral substances, are frequently present in varying amount.

Albumen in the Urine constitutes the symptom *albuminuria.* This is not *per se* diagnostic of organic renal disease. Recent investigation shows that it is a remarkably frequent, and at times persistent, symptom in many persons apparently in good health. Although undesirable, it cannot in itself be *always* regarded as a grave symptom.

The forms of albumen usually found in the urine are egg and serum albumen. Closely allied to these, but differing in some of their reactions are: —

1. The globulins, four in number; vitellin, myosin, fibrinogen, paraglobulin. They are insoluble in water, soluble in dilute neutral saline solutions.

2. Acid and alkali albumen. They are formed in the one case by the action of dilute acids, and in the other by alkalies on native albumen. Heat will not coagulate either of them, and each is soluble only in the solution designated by its name.

3. Peptone. This form is soluble in water, but is not coagulated either by heat, acids, or alkalies. It is not normally found in urine, but when present, the symptom is termed *peptonuria*. Formed as a result of gastric and pancreatic digestion, peptone may find its way into the urine through various channels resulting from suppurations. It is also said to be present in the urine when pus corpuscles are disintegrating anywhere in the body.

Furthermore, pus and seminal fluid contain a small trace of albumen. Mucin, although not precipitated from solutions by boiling, is coagulated by dilute acetic acid.

After all, it is only important to be familiar with serum albumen; further consideration of the other forms of albumen becomes unnecessary.

[As a constituent of the blood, albumen may appear in the urine as a result of hemorrhage or transudation from some portion of the urinary passages below the kidneys, — false albuminuria.]

*Detection.* — The most satisfactory clinical tests for albumen in the urine are the heat and nitric acid tests. The urine should be rendered perfectly clear by filtration. If it does not filter readily, it is customary to separate the earthy phosphates by the addition of ammonia. These, in falling, carry down the bacteria and other annoying substances, after which filtration is usually readily accomplished. Should the urine be already alkaline, it may be rendered filterable by the separation with the magnesian fluid of the alkaline phosphates.

*Heat Test.* — Albumen in solution is coagulable at about 70° C. Therefore, if a test tube half full of urine be heated carefully to a temperature just below the boiling point, albumen, if present, will be precipitated, and the clear solution rendered turbid or cloudy, according to the amount of albumen present. But heat is also liable, especially in urine whose reaction is close to the neutral line, to precipitate the earthy phosphates which may be mistaken for albumen. Hence it is customary to add a few drops of acetic acid, either before or after the heating, to keep the phosphates

in solution, and thus insure against such a source of error. If the acetic acid be added before heating, it is not unlikely that a slight precipitation of mucin will occur. If, on the other hand, the acid is not added, and on heating no coagulum appears, one step in the process has been saved. It is always advisable to confine the heating to the upper half of the fluid, as any cloudiness in this half, however slight, can thereby be readily compared with the clear, unheated portion below. In this way, the heat test becomes a fairly delicate means of determining the presence of albumen.

It should not be forgotten, however, that a few drops of *nitric acid* or an excess of acetic acid may convert the serum albumen into acid albumen, which is not coagulated by heat. Hence it may happen that (*a*) a precipitate of albumen may be dissolved by the addition of a few drops of nitric acid (although it reappears when an excess has been added), and (*b*) although much albumen is present it will fail to coagulate by heat if a few drops of nitric acid have been previously added. Although acid albumen is readily precipitated on neutralization with potassic hydrate, yet the least excess of alkali converts it into alkali albumen, and it redissolves. Hence it is dangerous to substitute nitric for acetic acid in this test.

*Nitric Acid Test.* — This test operates equally

well with serum, acid, or alkali albumen. It is also serviceable as an approximate quantitative test.

A collamore wine-glass is filled about half full of urine. To this is carefully added nitric acid, allowing the latter to flow down the side of the wine-glass, which is gently inclined to facilitate the operation. As the acid is heavier than the urine, it settles *en masse* in the lower portion of the glass, while the urine overlies it.

If albumen is present, it appears as a faint (or dense) white cloud or coagulum, forming a zone *between* the urine and the acid. To insure detection, after the addition of the acid it is well to hold the glass against some dark background, as the sleeve of a black coat. By so doing, very slight traces of albumen will not be overlooked.

If now the zone is thin, and, looking down upon it, quite transparent, the presence of a small amount of albumen ($\frac{1}{10}$ of 1% *by weight*, or less) may be assumed. Should the zone be thin (about the thickness of a crow-quill), opaque, but not flaky, it is indicative of about $\frac{1}{4}$ of 1%. Finally, if the zone is of the thickness of a goose-quill, opaque and flaky, the quantity is probably not far from $\frac{1}{2}$ of 1%. The maximum amount of albumen ever present in the urine is 3 or 4 per cent by weight.

The nitric acid test is valuable, clinically, for it not only indicates the approximate quantity of albumen present, but also betrays the presence of some other constituents as well. E. g. : —

1. In urine that contains an excess of urates, it is likely that another zone, *above* the albumen, (or where it would be if present,) will be observed. This zone, as suggested, consists of the mixed acid urates and uric acid that have been rendered less soluble by the addition of the nitric acid. This forms a sufficient clinical test for uric acid.

2. On the other hand, a zone in the nitric acid, *below* the albumen, consists of nitrate of urea, and is suggestive either of an excess of urea or a highly concentrated urine.

3. Should any bile pigment be present in the urine, between the urine and the acid the characteristic play of colors will be observed.

4. Having performed the test for albumen, in the same glass a drop of silver nitrate may be added, and any increase or diminution of the chlorides ascertained.

On account of the possibilities of error, it is always advisable, in testing for albumen, to perform both the heat and the nitric acid tests. By so doing, it is hardly possible to overlook the presence of albumen.

Under certain conditions, viz. in testing jaun-

diced urine, or where there is a large excess of urates present, it is preferable to employ the heat test. The same is also true when iodine or any resinous substance is present. If iodine is present, a brown-colored granular zone, which might easily mask a faint trace of albumen, is developed between the layers of acid and urine.

There are many other tests for albumen,—picric acid, sodium tungstate, nitrate of mercury (Millon's reagent), sulphate of copper (biuret), etc., —each serviceable in its own way; none of these, however, are of any clinical importance.

Finally, before testing for any of the normal constituents except the phosphates, it is well to remove any large excess of albumen.

Albuminuria may be renal (*true*), or non-renal (*false*).

True albuminuria depends mainly upon a disturbance either of blood pressure in the glomeruli, or of the nutrition of the glomerular walls. Any cause, therefore, that excites a disturbance of the diffusion membranes of the kidney, will be productive of albuminuria. Hence it happens that severe muscular or mental exertion, cold bathing on rising from bed, and even the ingestion of food, give rise to a temporary or "functional" albuminuria, that cannot be regarded as in the least pathological. Albuminuria of this

nature may be intermittent (i. e. every morning), paroxysmal, or even persistent.

Between the ages of fifteen and twenty there is frequently observed a temporary albuminuria associated with a physiological hypertrophy of the heart. This phenomenon is known as the *albuminuria of adolescence*, and is physiological.

When urine is passed in small quantity, of high specific gravity, and contains crystals of calcic oxalate, it is very liable to be slightly albuminous.

False albuminuria arises in consequence of hemorrhage into the urinary passages somewhere *below* the kidneys. It is essential, therefore, to bear in mind always the possibility of such a source of albumen.

Pathologically, albuminuria arises under a variety of conditions. In many instances it seems to be an associated symptom of general constitutional (especially febrile) disease, i. e. scarlet fever, diphtheria, and other disturbances of an infectious nature. In other cases, it appears to be associated with a true poison that is circulating in the blood, e. g. cantharides, iodoform, etc. In such cases, it is not unlikely that the albuminuria is due to irritation of the kidney caused by its attempt to eliminate the poison from the system.

Albuminuria appears, also, when for any reason the outflow of blood from the kidney is hindered,

e. g. in emphysema, phthisis, uncompensated valvular disease of the heart, and those conditions accompanied by general passive congestion; also in ovarian tumors, uterine tumors (pregnancy), or new growths, so situated as to obstruct the venous outflow of the kidney.

Finally, albuminuria is a most important symptom of organic disease of the kidneys themselves.

In acute parenchymatous nephritis during the acute or inflammatory stage, the amount of albumen in the urine varies from $\frac{1}{4}$ to $1\frac{1}{2}\%$. As the inflammation subsides and the amount of urine begins to increase, the albumen gradually diminishes to a trace, and finally disappears.

In chronic parenchymatous nephritis during the active stage, the amount of albumen is excessively large,—$\frac{1}{4}$–$4\%$ ordinarily $\frac{1}{2}$ to $2\%$. In the inactive stage it varies from $\frac{1}{4}$–$\frac{1}{2}\%$.

In chronic interstitial nephritis, the albumen rarely reaches $\frac{1}{2}\%$. It is usually $\frac{1}{4}\%$, more or less.

In amyloid degeneration of the kidney it begins as a mere trace, and steadily increases, —$\frac{1}{4}$–$\frac{1}{2}\%$ usually, but may rise as high as $3\%$.

In active hyperæmia of the kidneys, the amount varies with the blood pressure; usually less than $\frac{1}{4}\%$, oftener about $\frac{1}{10}\%$, but it may temporarily rise as high as $\frac{1}{4}\%$.

In passive congestion the amount varies with the degree of obstruction; i. e. anywhere up to ¼%, but it is rarely more than a trace.

SUGAR. — The presence of sugar in the urine constitutes the symptom *glycosuria.* It is doubtful whether sugar is a normal constituent of the urine. In health, however, the quantity present never exceeds $\frac{1}{10}$ of 1%, and in Trommer's test (*vide* page 58) it fails to make any impression upon the copper salt. Therefore this very small quantity may be disregarded. When the body contains an excess of sugar, it becomes a constituent of those fluids and tissues of the body normally free from it; at the same time, the amount of sugar in those tissues and fluids normally containing it is correspondingly increased.

There are several chemical varieties of sugar, namely, milk, cane, grape, and fruit, but that which finds its way into the urine is grape sugar. Grape sugar is also known under the name of glucose, dextrose, starch sugar, diabetic sugar, etc.

Pure grape sugar is as harmless an article of diet as any form of food, but it is not a satisfactory substitute for the common cane sugar.

Glucose is made by the action of sulphuric acid on starch; hence the name starch sugar. It turns polarized light to the right, and upon this fact is

based a most satisfactory, though expensive, quantitative test.

*Detection.* — The specific gravity alone, when 1030 or more, is quite suggestive of the presence of sugar; and if at the same time the urine is very pale, and exceeds 1500 c.c. in the 24 hours, the probability that sugar is present becomes almost a certainty. The only presumptive source of error is a large excess of urea.

*Moore's or Heller's Test.* — When heated with a fixed alkaline hydrate, grape sugar becomes a powerful reducing agent. Melassic acid is formed, and a deep brown color is imparted to the solution. If a few drops of nitric acid be added to this, the dark color vanishes, and an odor of molasses is liberated.

*Process.* — Pour into a test tube two volumes of urine and one of KOH, and heat to boiling. (If the earthy phosphates are present in excess, they may be removed by filtration.) Presently, if sugar is present, the dark color appears, and deepens on standing.

According to Bödecker, if a urine is treated with KOH and allowed to stand in the air, it gradually colors brown from above downward, because of the presence of a substance which he calls *alkapton.* Alkapton is a powerful reducing agent, and absorbs oxygen from the air. It will not reduce

bismuth salts, nor does it respond to the fermentation test. Hence, in performing the copper test, it may be necessary to remove the alkapton with basic acetate of lead.

*Trommer's Test.*—This is like the former, except that, before heating, a solution of cupric sulphate is added drop by drop, shaking after each addition until a beautiful azure-blue color is developed. Upon heating, the copper sulphate parts with some of its oxygen, and orange-yellow cuprous oxide is formed.

The precipitate must be obtained *without boiling.* Both of the above tests will react without heat, but they then require ten or twelve hours. Ammonium salts, urea, albumen, and organic substances generally, tend to hold the cuprous oxide in solution, and so interfere with the delicacy of the test. Then, again, other substances beside sugar act as reducing agents to the copper salt; viz. uric acid, urates, hippuric acid, hypoxanthin, mucus, indoxyl, urochloralic acid (after the ingestion of chloral), and turpenoglycuronic acid (when turpentine has been taken).

Inosit, or muscle sugar, is widely distributed throughout the body. Although not a normal constituent, it may make its appearance in the urine, either replacing or accompanying the grape sugar. It has been found in the urine of acute

nephritis, also in phthisis, syphilitic cachexia, and typhus fever. Inosit does not reduce the copper salt in solution with KOH, but in place thereof a green color is developed. Neither does inosit respond to the fermentation test (*vide infra*).

*Fehling's Test* is simply a modification of that suggested by Trommer, and is subject to the same sources of error. It is, however, the one commonly employed in making quantitative estimations of sugar. Fehling's solution consists of a solution of pure crystallized sulphate of copper (34.639 grm. to 200 grm. dist. water), to which is added, a little at a time, chemically pure neutral sodic tartrate (173 grm.) dissolved in 500 grm. of a solution of caustic soda (sp. gr. 1.12). The clear mixture is then diluted to a litre. 10 c.c. of this solution will be reduced by 50 milligrams of diabetic sugar. With a view to overcoming the extreme liability of Fehling's solution to decompose on keeping, it may be suggested that the solution of copper and that of the tartrate in the caustic soda be kept in separate bottles until required for use.

*Quantitative Estimation.* — Pour into a flask 10 c.c. of the freshly mixed Fehling's solution and 40 c.c. of distilled water. Place the flask with its contents on the sand bath, and heat to boiling. If the specific gravity is over 1030, the urine should be diluted 1:10; if under 1030, the dilution need

not be so great, e. g. 1:5. The diluted urine is then placed in a burette, the level of the fluid brought to the zero mark, and the beak of the burette inserted into the neck of the flask. Now, drop by drop, the urine is added to the boiling solution below, until the last trace of blue color disappears. (If, on boiling, the Fehling's solution changes color *before* the suspected urine is added, it will be necessary to obtain a fresh supply.)

The number of cubic centimeters of diluted urine used is then read off; e. g. 5 c.c. Inasmuch as the urine was diluted, say 1:10, there must have been ½ c.c. of undiluted urine used in performing the test.

Now, since 10 c.c. of Fehling's solution (the amount used) corresponds to .050 grm. sugar; the ½ c.c. of urine necessary to the reduction must therefore have contained just this quantity, viz. .050 grm. sugar. Hence 1 c.c. of urine will contain $.050 \times 2 = .10$ grm. sugar; or 100 c.c. 10 grm. = 10%. From these data the amount in 24 hours is readily calculated.

*Fermentation Test.* — By fermentation, sugar is broken up into alcohol and $CO_2$; therefore it is only necessary to cause fermentation in the urine, which can be done by the addition of a little yeast-cake. The $CO_2$ as it forms is passed through baryta water.

A more useful application of the fermentation test is in the so-called "Differential Density Method," suggested by Dr. Roberts. It is founded on the fact that (*a*) during fermentation diabetic urine suffers a diminution of density due to the destruction of the sugar; and (*b*) according to Dr. Roberts's observations each degree of diminution corresponds to one grain of sugar per fluid ounce.

*Process.*— Two four-ounce bottles are filled with saccharine urine. A small piece of yeast-cake is added to one, and the bottle, loosely corked, is put in a warm place. The other bottle is tightly corked, and placed in some cool spot. After standing two days, the specific gravity of the urine in each of the bottles is taken; then each degree of difference will represent one grain of sugar per fluid ounce. The percentage may be approximately determined from the result thus obtained by multiplying the number of degrees lost in the fermentation by 0.23.

Böttger's *Bismuth Test* is open to the objection of being too delicate. Sugar reduces nitrate of bismuth with the precipitation of metallic bismuth (black). All organic albumens contain sulphur, and are liable to cause the formation of black sulphide of bismuth, and so obscure the test. It is therefore imperative that, previous to performing

the test, all traces of albumen should be carefully removed.

Brüke's modification of the bismuth test is the most delicate of all. It is not, however, sufficiently practical to be given in this manual, and the reader is referred to more extensive works on the subject.

*Polarimetry* is one of the most reliable of tests, but the expense of the necessary instrument makes it unavailable for clinical practice.

The presence of sugar can, in most cases, be satisfactorily determined by Moore's, Trommer's, Fehling's, or Roberts's (fermentation) test.

Temporary glycosuria may be due to cerebral disturbance, carbonic acid poisoning, febrile disease, especially pneumonia, or to the exhibition of certain chemical substances, e. g. turpentine and chloral. It may also occur in nursing women after weaning, or when the milk is not removed with sufficient rapidity.

Pathologically, glycosuria characterizes the disease diabetes mellitus. The amount of urine passed in 24 hours is greatly increased. It is pale in color, clear when passed, acid in reaction, and of high specific gravity. Together with a varying amount of sugar (3 or 4 to 10 or 12 per cent), the normal solid constituents, although absolutely increased, are, by the excess of water, relatively

diminished. In this disease two or three pounds of sugar may be passed in 24 hours.

Saccharine urine, on standing, becomes cloudy and more or less opaque from the growth of the sugar spore, *Torula cerevisiæ;* but it does not become alkaline, and this is in part due to the presence of acetic acid, and in part to the fact that a film forms over the surface of the urine, and prevents the entrance of the ordinary fermentation spore, *Pencilium glaucum.*

In cases of glycosuria it is of importance to know whether the sugar in the urine varies with the amount ingested. For instance, during a period of fasting, the urine of a diabetic may contain a constant though very small amount of sugar, but upon resuming a starchy or carbohydrate diet this amount at once increases to 2 or 3%. Therefore, the increased glycosuria must be dependent upon the ingestion of food. Such cases are amenable to treatment, and the prognosis is not therefore wholly unfavorable. When, however, independently of diet, the glycosuria remains tolerably constant, the prognosis is unfavorable; for in such cases the sugar eliminated in the urine must be at the expense of the permanent tissues.

LEUCINE and TYROSINE are the decomposition products of the albuminous bodies or their derivatives. They appear to be present in the glan-

dular organs of the body,— liver, pancreas, and spleen, — especially when these organs are undergoing pathological changes. They are associated as a crystalline sediment in the urine whenever the oxidative processes connected with tissue metabolism are for any reason hindered; e. g. acute yellow atrophy of the liver, phosphorus poisoning (a few instances), typhus fever, and small-pox (occasionally).

### Abnormal Coloring Matters.

These may be distinguished as (*a*) those which occur normally in other fluids of the body, as the blood and bile; and (*b*) those which are the result of accidental excretion in the urine, viz. vegetable coloring matters. The latter were sufficiently treated under the physical properties of the urine. (*Vide* Color, page 16.) It only remains to state that their presence is readily recognized from the fact, that, on the addition of an acid, the urine loses its color, which returns, however, when an excess of ammonia is added.

Biliary Constituents. — When for any reason the bile cannot pass out of its channels into the intestine, it is reabsorbed by the blood, and eliminated by the kidneys, causing a discoloration of the urine, — an early symptom of jaundice. Clinically, only the coloring matters of the bile are

important. The bile acids are never present in any considerable amount, and their significance when found is entirely out of proportion to the difficulties in the way of detecting them, since Pettenkofer's test is not available.

The biliary pigments are several in number, and represent successive stages of oxidation through which the normal bilirubin passes. When present in excess, the urine is usually colored a deep brown or yellowish green, and when shaken with air a permanent froth of yellowish green color is developed. A piece of filter-paper or linen, moistened with jaundiced urine, is permanently stained yellow.

Bilirubin is always obtained from biliary calculi, in which it exists as a salt, insoluble in alcohol, chloroform, or ether. Cholesterine is separated by heating with ether, the lime is decomposed by the addition of hydrochloric acid, and bilirubin is freed.

Jaundiced urine, when acidulated and shaken with chloroform, yields the biliary pigments to that reagent.

Alkaline urine containing bile pigment turns green upon standing, owing to the formation of biliverdin from bilirubin by the absorption of an atom of oxygen.

*Gmelin's Test* consists simply in oxidizing the bilirubin with $HNO_3$ (the more impure, the better).

The result is a play of colors in the following order: green, blue, violet, red, and yellow. It has already been noticed (*vide* page 52) how the test may be obtained during the nitric acid test for albumen, and generally the presence of a little albumen rather improves the test. Before applying the nitric acid test, a very dark urine should be diluted with water.

Another method is to add to a little urine, spread on a small porcelain dish, a drop of nitric acid. Prismatic rings of color are developed as above.

There is no pathological increase of pigments. Their presence is indicative of jaundice, but they give no information as to the cause of the jaundice.

Bile pigments adhere very readily to precipitates; hence amorphous urates and the earthy phosphates precipitated from biliary urine are colored brown.

Coloring Matters of the Blood. — An admixture of blood with the urine is easily recognized, unless the amount be very small, by the color. Hæmoglobin is readily decomposed, by reducing agents and acids, to hæmatin and globulin (or globin). Hæmatin imparts a brown color to its solution. In an intermediate stage, methæmoglobin is formed, and this substance gives to its

solution a darker shade of red than hæmoglobin. According, then, as it is unaffected, or has undergone decomposition, hæmoglobin imparts to the urine a blood-red, brownish, or dark brown tint.

Blood may enter the urine at any point, from the glomeruli to the external meatus. Naturally, that which enters the urine during its passage through the kidney, e. g. hæmorrhages from the renal capillaries, is longer retained in the urine at the body temperature. This fact, combined with the absence of oxygen and the presence of carbonic acid, favors the decomposition of the blood to methæmoglobin and hæmatin, and the urine is therefore colored dark brown. The blood that enters the urine below the kidneys is less liable to undergo decomposition, and from this fact it follows that the urine is more liable to be blood-red in color. As the blood undergoes decomposition, intermediate shades of color, according to the stage of decomposition, exist; and in order that the above distinction as to probable source may be made intelligently, it is necessary to observe the color of the urine *at the time* it is passed.

Blood pigment in the urine may or may not be accompanied by the corpuscular elements. Rupture of the vessels, by which all the constituents of the blood escape into the urine, gives rise to the symptom *hæmaturia*. In such cases, the globules,

deprived more or less of their pigment, are detected in the sediment, while the colored urine betrays the presence (in solution) of the liberated pigment.

In some diseases (*vide infra*) the blood is decomposed while yet within the vessels, and upon its arrival in the kidney the pigment that has been liberated by this internal decomposition finds its way into the urine. Thus, the presence in the urine of the pigment, unaccompanied by corpuscular elements, gives rise to the symptom of *hæmoglobinuria.*

Hæmoglobinuria is a symptom of scurvy, purpura, scarlatina, and profound malarial poisoning. It also occurs in septic and pyæmic diseases, after the transfusion of blood from an animal of another species, after the inhalation of arseniuretted hydrogen, after severe burns, and after poisoning by many substances, viz. hydrochloric, sulphuric, and carbolic acids, and chlorate of potash. The urine is highly albuminous, colored brown, and in addition contains an abundant sediment of amorphous matter.

Like bile pigment, hæmoglobin attaches itself to any precipitate; e. g. if the albumen is coagulated, it is colored a distinct brown. At the same time, the urine loses the color due to the presence of blood, and assumes its otherwise normal tint.

Undecomposed hæmoglobin, together with methæmoglobin and hæmatin, may be detected with the aid of the spectroscope, or, if the quantity to be examined is very small, the microspectroscope. Oxyhæmoglobin gives rise to two absorption bands, one in the yellow and the other in the green portion of the spectrum (i. e. between Fraunhofer's lines D and E), while reduced hæmoglobin gives only one band, situated between the two, which is fainter but broader than either of them.

The disintegration of blood corpuscles within the body is accompanied by an increased activity of the liver. As a result of this, a larger quantity of bile pigment is secreted, which is eliminated in the urine with its usual pigmentary effect (*cf.* Urobilin).

Tests for the Detection of Blood. — *Teichman's test* is very delicate. It is based on the fact that when hæmoglobin is decomposed, hæmatin is formed. The latter readily unites with the halogens (Cl, Br, I) to form hæmin, the crystals of which are characteristic, and easily identified under the microscope.

*Process.* — The earthy phosphates, to which the blood pigment readily attaches itself, are precipitated and filtered out, dried, and a small quantity placed on a slide. To this are added a few

grains of common salt, and the two are then thoroughly mixed. A hair is next laid across the mixture, and a cover-glass superimposed. A little glacial acetic acid is allowed to flow under the cover-glass, and the slide carefully warmed, until, under the cover, little bubbles appear. The slide is then set aside, and while it cools crystals of hæmin form, which, as stated above, may be detected under the microscope. If, from too prolonged heating, the crystallization is imperfect, a little more distilled water may be added, the slide warmed again, and then set aside for recrystallization.

*Sodium Tungstate Test.*— The urine is strongly acidulated with acetic acid, sodium tungstate added, and heat applied. A chocolate-brown precipitate falls, with which Teichman's test is performed as above.

*The Heat Test.*— Coagulation of the serum albumen may be useful as a confirmatory test for blood. A drop of the suspected urine is placed on a glass slide and carefully heated. Coagulation of the albumen takes place, as in the heat test for that substance.

*The Iron Test* is based on the fact that blood contains a little iron. The suspected precipitate is dried, and after ignition hydrochloric acid and potassic sulphocyanide are added. If iron is present

(i. e. blood), a deep blood-red color is developed (ferric sulphocyanide).

In cases of hæmaturia, the discovery of the corpuscles with the aid of a microscope is the most reliable means of demonstrating the presence of blood in the urine. It should not be forgotten, however, that in very dilute or ammoniacal urine the blood disks may be dissolved, and so disappear quite rapidly. Hence failure to detect them does not invariably imply that they never were present in a given specimen.

As will be shown in the chapter on sediments, the red blood globule, as found in urinary deposits, varies in its optical appearances. It may be *normal*, or, owing to certain conditions (e. g. the presence of salts), distinctly *abnormal.*

The microscopic test not only confirms the presence of blood, and indicates its condition, i. e. whether normal or abnormal, but it also enables the skilled observer to determine from what animal the blood in question was derived. This follows from the fact that in different animals the diameter of the red corpuscle varies. In all the mammalia, except the camel and llama, the red corpuscle is circular or disk-shaped, and without a nucleus. In the cases just mentioned as exceptions, it is also non-nucleated, but oval in outline. On the other hand, in birds, reptiles, and fishes, it is both oval and nucleated.

The following table shows the average diameter of the blood disks of a few mammalia.

| | | | |
|---|---|---|---|
| Human, . . . . . | $\frac{1}{3200}$ inch. | | |
| Goat . . . . | $\frac{1}{3100}$ inch. | Horse . . . . | $\frac{1}{4600}$ inch. |
| Sheep . . . . | $\frac{1}{5000}$ " | Pig . . . . . | $\frac{1}{4350}$ " |
| Dog . . . . . | $\frac{1}{3580}$ " | Cat . . . . . | $\frac{1}{4400}$ " |
| Rabbit . . . . | $\frac{1}{3600}$ " | Squirrel . . . | $\frac{1}{4000}$ " |

For the purpose of measuring accurately the diameter of the disks, a microscopic slide, on which are ruled parallel lines $\frac{1}{1000}$ of an inch apart, is used. The blood to be measured is placed on this slide and examined under a microscope, the ocular of which contains a scale so ruled that ten of its parallel lines correspond to the space between any two lines of the slide. Thus, a measurement of $\frac{1}{10000}$ of an inch is readily made, and the diameter of the globule in question easily determined.

The best menstruum for preserving and mounting blood globules for measurement is acetate of potassium.

### Accidental Constituents.

Fat. — This may occur, in general, in one of four ways: — 1. The result of fatty degeneration of the cells lining the renal tubules. (A most important source.) 2. By the immediate connection of the lymphatics with the urinary passages, giving rise to the so-called chyluria (*vide* next page). 3. By the direct separation of fat, as

a result of renal activity. This occurs, but rarely, among pregnant women, and those taking a large amount of cod-liver oil. 4. By the accidental or intentional addition of extraneous fat, as may happen after the passage of greased catheters and sounds; from the use of old hair-oil bottles for transporting urine, etc. Hysterical patients may add oily substances to their urine for the purpose of deception.

Fat is usually detected by its microscopic appearances: globular outline and strongly refracting border; but even then it may at times (e. g. chylous urine) be a matter of some difficulty. Bubbles of air, too, often simulate fat globules extremely well.

In the later stages of acute disease of the kidney fat may be present for a short time only. It is, however, a prominent symptom throughout the entire course of chronic renal disease; e. g. chronic parenchymatous nephritis.

Fat may be present in the urine in a state of very minute subdivision, as in *chyluria.* Such a urine is spoken of as "chylous." It is milky white in color, and the milkiness persists even on standing. Out of contact with the air, the fat does not separate out; but on exposure decomposition takes place, with the separation of the fat, which then rises to the surface.

The addition of milk to normal urine produces an appearance resembling chyluria; but under the microscope the fat globules of milk can be distinguished, whereas those of chylous urine cannot. If chylous urine is shaken with ether, the ether takes up the fat. This is not so with milky urine, since the fat globule of milk is coated with an albuminoid substance that must first be dissolved by the addition of an alkaline hydrate.

Fat forms about 1% by weight of chylous urine. Besides the fat, considerable mucus, leucocytes, and blood globules are present. As elsewhere suggested, the presence of chyle in the urine is probably due to a communication between the lymphatics and some point of the urinary passages. The communication is said to be effected by the action of a parasite, *Filaria sanguinis hominis*, which has been found in the blood of those afflicted with the disease. The affection is quite common in the tropics, where it appears to be endemic.

At times chyluria appears to be intermittent, i. e. occurring only in the morning, while during the remainder of the day the urine is passed clear.

*Cholesterine* may, though very rarely, be associated with fat. Its presence in the urine is of little known significance, and of still less importance.

*Acids of the Fatty Series* — formic, acetic, propionic, butyric, etc. — are found in urine, but only

in very small amounts. Acetic acid is present in the stage of acid fermentation, and in saccharine urine after fermentation has begun. In the latter instance, it is this acid that, in connection with the surface film (*vide* page 63), helps to prevent the urine from becoming alkaline. Butyric acid may be found in diabetic urine after the addition of chalk. The decomposition of leucine may give rise to the presence of valerianic acid.

*Of the Organic Acids which are not Fatty*, lactic acid is present in urine in two forms. In diabetes, the ordinary lactic (milk) acid is present; but under certain circumstances sarcolactic acid may appear. The only means of distinguishing the two forms lies in the fact that sarcolactic acid forms salts with zinc and calcium.

Lactic acid is present, whenever the oxidative processes of the body are hindered, and therefore usually in connection with leucine and tyrosine; viz. acute yellow atrophy of the liver, poisoning by phosphorus and arseniuretted hydrogen, typhus fever, and severe cases of small-pox.

Benzoic acid is found in the urine of herbivora in abundance, as a result of the decomposition of hippuric acid.

*Ammonia Compounds.* — Ammonia is normally present only in very small amount (1%). By diet and the decomposition of nitrogenous tissues some

variation in this amount may be induced. Carbonate of ammonium appears in urine as the result of the decomposition of urea. Sulphide of ammonium may appear whenever putrid suppuration is going on.

Pus contains sulphur compounds, which, upon decomposing, it liberates. In any disease not connected with the urinary apparatus, the presence in the urine of sulphuretted hydrogen may be regarded as a favorable sign.

*Alkalies* are present normally, and also as a result of medication. By the processes of body metabolism, citrates, tartrates, etc. are converted into and eliminated in the urine as carbonates.

*Iodide of Potassium* may be detected when present by the nitric acid test for albumen. Between the two layers (urine and acid) a delicate brown-colored zone is formed (*vide* page 52).

*Extraneous substances*, such as articles of food and drink, also various medicines, may get into urine, either accidentally or voluntarily (hysterical patients). As possible sources of urine contamination, they should constantly be borne in mind.

*Various metallic salts*, principally those of lead, arsenic, and mercury, are eliminated in the urine. In cases of suspected poisoning, their detection forms a very important set of urino-chemical analyses.

LEAD. — Unless means be taken to secure its removal, the lead that is absorbed accumulates in the system as a fixed constituent of the tissues. The natural channel of elimination is by way of the kidneys and urinary passages. In order that it should become a constituent of the urine, the lead must first be converted into a compound that is soluble in the blood. This is best effected by the administration of iodide of potassium. As this salt mingled with the blood circulates among the tissues containing lead, the latter is converted into plumbic iodide, a salt that is somewhat soluble in water at the temperature of the body, and is then carried by the blood to the kidneys, and eliminated as a constituent of the urine. Even under these circumstances, only a few milligrams of lead are eliminated in the twenty-four hours. It follows that, in order to detect its presence, a very large quantity of urine should be examined, and in the process of analysis every precaution taken to prevent the accidental addition of even the slightest quantity of extraneous lead.

*The Analysis.* — A litre of urine is evaporated over the water bath to dryness. When nearly dry, the residue is moistened with nitric acid. When effervescence has ceased, the bright yellow residue is transferred while hot to a platinum crucible, thoroughly heated, and ignited. The crucible

with its white residue is then placed in a dish of hot dilute hydrochloric acid to dissolve the slag. The solution is filtered while hot, and the filtrate treated with an excess of ammonia water and ammonium sulphide. This precipitates the phosphates and sulphides of iron and lead. After standing over night the precipitate is washed several times, by decantation, with boiling water, and an excess of hydrochloric acid added to dissolve the phosphates and sulphides of iron. After standing again over night, the sulphide of lead settles, and is then collected on Swedish filter-paper. The black sulphide of lead is washed with boiling water on the filter, after which boiling dilute (chemically pure) nitric acid is added, drop by drop. The sulphide dissolves and is collected in a watch-glass. This is then evaporated to dryness over the water bath; the result of which is a white residue of basic nitrate of lead.

A preliminary test is first made by placing a crystal of the white residue in a watch-glass, and, after moistening with a drop of water, a crystal of potassic iodide is moved about in it. A yellow streak indicates the presence of some metal, probably lead. The confirmatory test is performed as follows. The white residue (basic nitrate of lead) is dissolved in a drop or two of acetic acid, and washed with hot water through a filter-paper into

a test tube. To this a drop of sulphuric acid is added, and by the next day sulphate of lead has formed.

ARSENIC. — The amount of arsenic eliminated in a litre of urine is very small; hence, in the analysis for that metal, a considerable quantity of urine is necessary.

*Process.* — One or two litres of urine are evaporated to dryness, moistened with nitric acid, and ignited (as in analysis for lead). The white residue from ignition is treated with dilute sulphuric acid, and heated strongly over a sand bath to expel any excess of nitric acid. The nitrates are converted by the process to sulphates, and these are extracted by water. The solution is then filtered, and the filtrate received into a Marsh's apparatus which has been previously tested and found to be free from arsenic.

MERCURY. — The urine is first concentrated to half its volume, and then acidified with dilute hydrochloric acid. In this is suspended a platinum wire, to which is attached a bit of iron. After an hour or two, metallic mercury is deposited on the wire. The wire is then removed, rinsed with water, and suspended in an atmosphere of chlorine gas, by which the metallic mercury is converted into corrosive sublimate. The wire is then pressed between the fold of a paper which has been pre-

viously moistened with iodide of potassium. If mercury is present, a scarlet streak of mercuric iodide ($HgI_2$) is left on the paper wherever it came in contact with the wire.

## CHAPTER III.

### THE SEDIMENT.

A TURBIDITY of the urine arises from the fact that it may, and often does, contain substances that are more or less insoluble in it. So long as these substances remain diffused through the fluid, turbidity persists. After a time, however, varying with the consistency of the urine and the weight of the insoluble matters, the latter gradually settle to the bottom and form a sediment. In urinary examinations, the quantity of the sediment is usually reported as *little* (*slight*), *considerable*, or *much*.

The constituents of the sediment are eliminated from the body in the urine, either as such (i. e. already separated), and have therefore only to settle, or, as the result of certain changes presently to be described, they may appear only after the urine has been passed. The changes referred to pertain more especially to the reaction of the urine, which after elimination undergoes modifications and change.

When freshly passed, the acidity of normal urine is such that the solid inorganic constituents are

kept in perfect solution. It has already been shown elsewhere, that certain of the urinary constituents, by the existence of a reaction other than of normal degree or kind, are rendered insoluble, and appear as deposits. Hence it follows that any considerable deviation of reaction from the normal will be followed by a precipitation of those constituents which are insoluble in urine of that reaction. Such changes of reaction may occur while the urine is yet within its natural channels (uric acid diathesis and cystitis), or only after it has been voided (fermentation).

### Fermentation of the Urine.

When freshly passed, normal urine is perfectly clear; but after standing a short time there appears, floating somewhere between the top and bottom of the fluid, a faint nebula or cloud, composed of the mucus and exfoliated epithelium which, as the urine flows outward, are carried along with it. After longer standing, this nebula increases in volume and density, and finally settles to the bottom. The acidity of the urine, as well as the intensity of its color, has at the same time increased. In fact, the urine has undergone the so-called "acid fermentation."

Two views are entertained with regard to the cause of the increased acidity. One theory is

based on the tendency that exists between the acid sodium phosphate and normal urates to mutual decomposition, viz.: —

1. $Na_2\bar{U} + NaH_2PO_4 = Na_2HPO_4 + NaH\bar{U}$.
2. $NaH\bar{U} + NaH_2PO_4 = Na_2HPO_4 + H_2\bar{U}$.

Thus the acid sodic phosphate takes away a part of the base of the normal urate, and leaves the acid urate, which is less soluble than the normal salt. It is to the separation of this salt that the increase of the mucous cloud mentioned above is in part due. This reaction occurs especially at a low temperature; but if the temperature be high, and at the same time there exists in the urine an excess of the acid sodic phosphate, the decomposition goes a step further. The acid urate salt is entirely deprived of its base, and the almost insoluble uric acid separates out as beautiful distinct crystals, which are reddish or reddish brown in color, and fall to the bottom as a granular powder. At times the uric acid is mixed with the amorphous undecomposed urates, forming the so-called brick-dust or lateritious sediment.

The second theory is based on the fact that the coloring matters, through the agency of the mucus of the bladder acting as a ferment, are converted into acetic and lactic acids. These then react upon the normal urates in the same manner as the

acid phosphate of sodium, and with the same results. Sufficient proof that the fermentation assumed in this theory takes place is wanting, and therefore the first theory seems on the whole the more probable.

When the changes described take place within the urinary passages, the urine, when passed, is turbid, and the sediment is spoken of as "gravel or sand." Such a condition is pathological, and paves the way to serious urinary disturbances.

Mixed with the sediment that has fallen, as a result of the changes described above, are often found crystals of calcic oxalate. A part of the uric acid is in the organism changed to oxaluric acid, which on exposure to air becomes oxidized to oxalic acid, and appears in the sediment as calcic oxalate.

When the decomposition between the urates and phosphates has ceased, there follows, after an interval which is much shorter in hot weather than in cold, a new process, — a true fermentation. The color of the urine becomes paler, the reaction gradually less acid, neutral, and then alkaline. As a result of these changes, the uric acid and urates disappear and give place to a new series of salts, — phosphates of the alkaline earths. The odor becomes distinctly ammoniacal and then putrid, while the turbidity, now due to the presence

of the alkaline phosphates and ever increasing mass of bacteria, constantly increases.

To what the alkaline change is due, is a matter upon which authorities differ (*vide* Reaction, p. 18). According to some, it is believed that decomposing mucus liberates a ferment in the presence of which urea is decomposed. Others are inclined to regard the change as a species of bacterial fermentation, while the remainder are inclined to the view that it proceeds from the action of a definite substance or ferment, which can be isolated from alkaline urine (Musculus ferment, *vide* page 19).

However effected, the fact remains that it is a true fermentative process, in which urea is decomposed to carbonate of ammonium, and it is to the formation of this substance that the alkaline reaction is due.

The ammonia can combine with uric acid to form urate of ammonium, which, unlike the other normal urates, is quite insoluble. This salt appears in the sediment when ammonia is being set free, i. e. just at the beginning of the alkaline change, and before it joins with the magnesic phosphate to form the triple or ammonio-magnesic phosphate.

Thus the changes in the sediment corresponding to the alkaline fermentation consist on the one hand in a disappearance of the salts formed in the

course of the acid fermentation, and on the other in the appearance of urate of ammonium (in the early stage), amorphous phosphate of lime, and triple phosphate, together with large quantities and numerous varieties of bacteria.

As in the acid fermentation, so also in the alkaline, the change may take place within the body, i. e. pelvis of the kidney or bladder, and thereupon give rise to pathological conditions associated in the first instance with gravel or calculus, and in the second with irritation and inflammation, especially of the bladder.

### Classification of the Sediment.

Urinary deposits have been classified by different writers according to their physical characteristics, their nature and origin, and the reaction of the urine in which they are found. The simplest of these classifications is the second, in which the sediment is regarded either as organized or not organized.

The organic deposit embraces all those organic forms which are insoluble in the urine, whether it is acid or alkaline. They are never normally present in urine, and when present are merely suspended in it, sinking more or less slowly to the bottom, and forming a part of the sediment.

The non-organic deposit includes those substances which, for the most part, exist in the urine

in a soluble state. When for any reason, e. g. excessive quantity or a change in the reaction of the urine, they are rendered insoluble, these substances are precipitated in a crystalline or amorphous condition.

Following the classification suggested above, these substances may be tabulated as follows: —

| Non-organized. | Organized. |
|---|---|
| Uric acid. | Mucus. |
| Urates { Na. K. $NH_4$. Ca and Mg. | Epithelial cells. |
| Amorphous urates (mixed). | Leucocytes and pus. |
| Hippuric acid. | Blood corpuscles. |
| Calcic oxalate. | Fibrin. |
| Amorphous phosphates (mixed). | Renal casts. |
| Calcic phosphate. | Spermatozoa. |
| Triple phosphate. | Fat. |
| Calcic carbonate. | Fungi. |
| Cystine. | Morbid growths. |
| Xanthine. | Entozoa. |
| Cholesterine. | Extraneous matter. |
| Leucine. | |
| Tyrosine. | |
| Bilirubin (Hæmatoidin). | |

## Uric Acid and Urates.

Uric acid, as has been said, exists in normal urine in combination with the alkaline bases, but under certain conditions it is itself precipitated as a reddish-colored deposit of small bulk, sinking to the bottom, or at times floating on the surface, and also adhering to the sides of the glass.

Uric acid is found only in *acid* urine (*cf.* Acid Fermentation, page 83). Causes contributing to its separation are those which induce a concentration of the urine, an increase of its acidity, or a pathological increase of uric acid. Uric acid and its salts when precipitated carry down the coloring matters present in the urine, and are therefore colored, usually a light yellow, varying to dark brown, or under certain conditions amethystine. Pure uric acid is, however, white and amorphous. Owing to their free solubility, normal urates, except the ammonium salt, which is insoluble, are almost never present in sediment. The acid and its acid salts, however, are much less soluble, and therefore appear as very common constituents of urinary deposits.

*Recognition.* — The typical or primary shape of uric acid crystals may be said to be a rhombic plate, to which the various forms met with may be referred. The angles and sides may be about equal, giving rise to quadrangular tables or cubes; more frequently two opposite angles are rounded off, by which ovoid or whetstone crystals are obtained; again, two opposite angles may be cut off smoothly, and so give rise to the hexagonal forms. Elongation produces a rod, and when many of these are joined about a common centre, fan-shaped to complete star forms are produced. Many other

atypical forms occur, whose recognition practice makes easy.

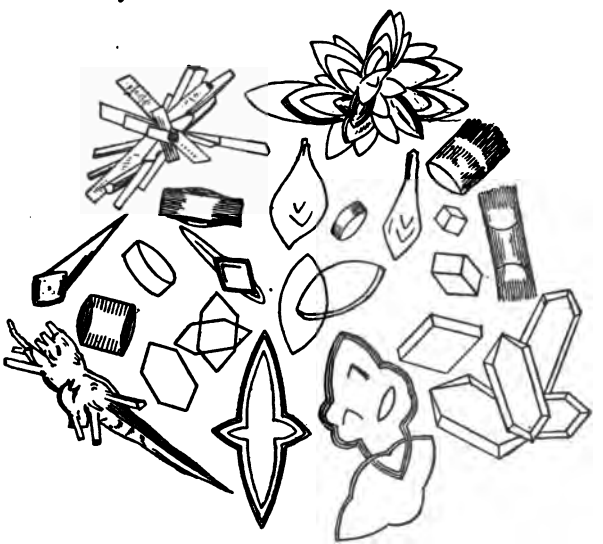


FIG. 2. Various forms of Uric Acid Crystals.

In general, crystals of uric acid are almost always colored, insoluble in acids and hot or cold water, but soluble in alkaline hydrates. Finally, they respond to the murexide test (*vide* page 31). The hexagonal modification may be mistaken for cystine, but cystine is colorless, and soluble in hydrochloric acid. The elongated rhombic prisms sometimes met with may be mistaken for crystals of triple phosphate, but the latter are colorless,

found only in ammoniacal urine, and are soluble in dilute acid.

Urate of ammonium, as mentioned above, is an exception to the free solubility of the normal urates. It is very insoluble, and appears in urine after the liberation of ammonia has begun, i. e. at the beginning of the alkaline fermentation. It is the only urate found in alkaline urine, and crystallizes in the form of brown-colored spheres, either single

FIG. 3. Spherules and Spiculated Spherules of Ammonium Urate and Amorphous Granular Urates. In the upper portion of the circle are Prismatic Crystals of Acid Sodium Urate.

or double, and with smooth or spiculated surfaces. The characteristic appearance of the spheres when studded over with spines has given rise to the

names hedgehog and thorn-apple crystals. If the spines are variously bent and distorted, a great variety of forms is produced. The elimination through the urinary passages of such crystals as these is frequently a cause of great irritation and pain. They may lead to the formation of calculi, and are commonly found in children whose urine is charged with renal calculi.

The acid ammonium urate occurs only in alkaline urine, together with the earthy and triple phosphates.

The acid urates are dissolved by heat and the alkalies; also by dilute acids (e. g. dilute HCl) with subsequent crystallization of uric acid. They also respond to the murexide test.

Occasionally the urates of sodium and potassium are crystalline, and appear in the sediment in forms resembling sheaves of wheat or delicate rosettes.

The other urates (mixed) usually occur as a loose, amorphous, pulverulent reddish deposit (brick-dust sediment), separating usually after the urine has been passed. The color, of course, depends on the presence and intensity of the coloring matters in the urine from which the urates are deposited. Microscopically, the deposit is indistinguishable from other fine granular matter, and therefore requires chemical tests to determine its nature. When attached to delicate shreds of mu-

cus, the amorphous urates may simulate fine granular casts. With a little familiarity, however, their true nature is readily determined.

The amorphous urates are soluble in hot, but insoluble (or less soluble) in cold water; hence it happens that they often separate after the urine has cooled considerably below the body temperature (as in cold rooms during the winter). The separation is of course more likely to occur whenever there is a relative or absolute increase of the uric acid (concentrated and fever urines).

### Hippuric Acid.

In conjunction with uric acid, and under conditions elsewhere stated (*vide* page 33), hippuric acid appears in the form either of prismatic acicular needles, or more commonly of semi-transparent quadrilateral prisms, with two or four bevelled surfaces at their ends. They are distinguished from uric acid by the fact that they are colorless, do not respond to the murexide test, and are soluble in boiling alcohol. (Uric acid is not dissolved by boiling alcohol.)

### Calcic Oxalate.

Among the oxidation products of albuminoid substances (*vide* Acid Fermentation, page 84) is calcic oxalate. In sediments, calcic oxalate crystals usu-

ally occur in two typical forms, i. e. quadrilateral octahedron and dumb-bell. The former is the more common form met with, and may be said

FIG. 4. Various forms of Calcic Oxalate Crystals.

to consist of two low four-sided pyramids joined at their bases; hence their appearance varies according to the position in which they are viewed, e. g. envelope and diamond. Occasionally the two pyramids are joined by an interposed quadrilateral prism. In disintegrating, this part disappears first.

The dumb-bell form is highly characteristic, and requires no further description. It may be mentioned, however, that when seen end on, these

dumb-bell forms suggest oval-shaped crystals and biconcave disks, not unlike blood globules.

Normally oxalic acid tends to undergo complete oxidation to carbon dioxide and water. It is also somewhat soluble in acid sodium phosphate; hence the small amount usually present is held in solution. The amount of oxalic acid in the urine is increased by any interference with the normal oxidative processes, or by the ingestion of oxalic acid in any form, e. g. rhubarb, garden sorrel, tomatoes and other vegetables, and carbonized drinks. Oxaluria, when persistent, gives rise to nervous symptoms somewhat analogous to those of nephritis, and it is therefore at times called "false Bright's disease."

Finally, when separating in the renal tubules, the calcic oxalate crystals give rise to considerable irritation; the crystals become agglutinated in the consequent increased mucus secretion and so form the nuclei of renal calculi.

*Optical and Chemical Characters.* — The only crystals with which calcic oxalate may be confused are the triple phosphate. The latter, however, occur only in alkaline urine, and are readily dissolved by acetic acid, whereas calcic oxalate occurs only in acid urine and is unaffected by acetic acid.

Crystals of uric acid and calcic oxalate are best preserved by washing (by decantation) with acetic acid.

## Earthy Phosphates.

These consist of the phosphate of lime (amorphous, $Ca_3(PO_4)_2$, crystalline, $CaHPO_4$), and the ammonio-magnesian or triple phosphate ($MgNH_4PO_4 . 6\ H_2O$). They occur as a bulky white opaque deposit only in feebly acid or alkaline urine, and most abundantly in the urine of alkaline fermentation. The ingestion of vegetables which are largely alkaline is productive, within an hour or two, of a neutral or faintly alkaline urine, in which, if voided soon after a meal, is discovered a precipitate composed of earthy phosphates in an amorphous condition. In this state they do not tend to form calculi.

The application of heat will at times, even in a slightly acid urine, by driving off the carbonic acid in which they are somewhat soluble, cause a precipitate of phosphates which may be mistaken for albumen. The addition of acetic acid, however, will cause a solution and disappearance of the phosphates.

The crystalline form of the phosphate of lime resembles very closely that of the acid urate of sodium (i. e. rosette form). It occurs in weakly acid urine, either alone, or, as in alkaline urine, more commonly associated with the triple phosphate.

Triple phosphate requires for its crystallization

the presence of ammonium compounds; hence it is rarely found until the urine has, by the decomposition of the urea, become ammoniacal. The triple phosphate crystal is easily recognized as a triangular prism with bevelled ends. Owing to their characteristic shape, these crystals are also called "coffin-lid." Modifications occur in which one or


FIG. 5. Coffin-lid Crystals of Triple Phosphates; Feathery Star-shaped Crystals of the same At *a* is a group of Crystalline Phosphate of Lime.

more corners are wanting, or the body of the crystals is variously shortened. Such forms may be confused with calcic oxalate crystals, but may be distinguished as already stated (*vide* page 94).

Occasionally, as when precipitated rapidly, beau-

tiful star-shaped feathery crystals of triple phosphate are found.

As a result of the alkaline changes that occur under certain conditions within the bladder, the earthy phosphates are deposited upon calculi of uric acid, calcic oxalate or ammonium urate.

All the phosphates are soluble in acetic acid, whereas those salts resembling them are not. In case of doubt, this makes a ready test.

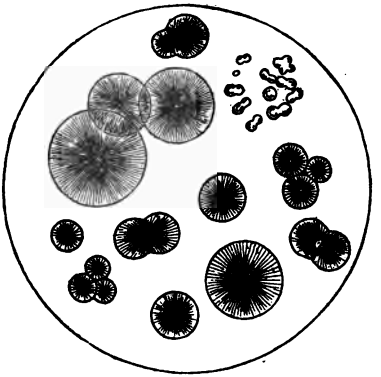


FIG. 6. Spheres and Dumb-bells of Calcic Carbonate from the Urine of the Horse. (Roberts.)

## CALCIC CARBONATE.

Crystals of this salt do not appear as an independent sediment, but associated with the earthy phosphates. Abundant in the urine of herbivora,

it is present only exceptionally in man. Occurring usually as a fine-grained powder, it may assume a crystalline form not unlike urate of ammonium. It is, however, colorless, and upon the addition of mineral acids an effervescence occurs.

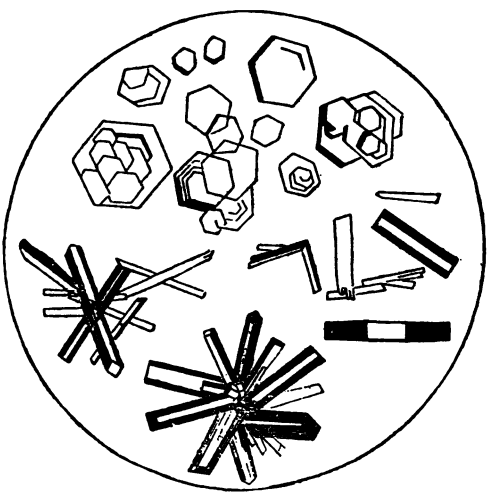


FIG. 7. Cystine: Hexagonal Tablets and Prisms from an evaporated Ammoniacal Solution. (Roberts.)

## CYSTINE.

Cystine is a crystalline body of considerable rarity. It is found only under certain abnormal conditions of the body, which are as yet but imperfectly understood. The fact that it contains

about 26% of sulphur suggests the possibility that it may be a vicarious secretion of taurin.

Many instances are recorded in which cystinuria appears to be hereditary.

Cystine crystallizes in regular hexagonal tablets of varying size, appearing either singly or in superimposed series. The latter may be made up of crystals whose size diminishes in an ascending series, or of crystals which overlap each other like shingles on a roof. At times the opposite angles of the crystal are joined by lines passing through a common centre. Roberts mentions the occurrence of square prisms of cystine which refract light strongly, and in connection with the hexagonal form appear either singly or in stellate aggregations.

Like many other crystalline sediments, cystine is strongly disposed to separate inside the urinary passages and there give rise to calculi; in this form cystine is more often found.

Cystine can only be confounded optically with a pure, colorless, and exceedingly rare form of uric acid. By reflected light, however, the uric acid has a yellowish tinge, whereas cystine has an iridescent mother of pearl lustre.

*Chemical Characters.* — Cystine is soluble in hydrochloric, but insoluble in acetic acid; hence the addition of the latter will precipitate cystine. It is

also soluble in ammonia, and the hydrates and carbonates of the fixed alkalies. By evaporation of the ammonia solution, beautiful hexagonal crystals of cystine may be obtained. If uric acid resembling cystine is dissolved in ammonia, then upon evaporation characteristic crystals of ammonium urate are formed.

### Xanthine.

Xanthine is a very rare constituent of the sediment. Like cystine, it occurs oftener as a constituent of calculi than as an independent crystal. It is so rare, that further consideration may be omitted.

### Cholesterine.

Cholesterine, a crystalline derivative of fat, is an infrequent constituent of urinary sediments. It occurs in the form of long quadrangular plates of various sizes (Fig. 8), and is said to be present in fatty degeneration of the liver, and in cheesy cystic degeneration of the kidney

### Leucine and Tyrosine.

In sediments these substances usually appear together, and since they accompany only grave destructive diseases of the liver — acute yellow atrophy and phosphorus poisoning — the urine is usually highly charged with bile pigment.

When their presence is suspected, simple concentration alone is sufficient to produce a sediment of leucine and tyrosine crystals.

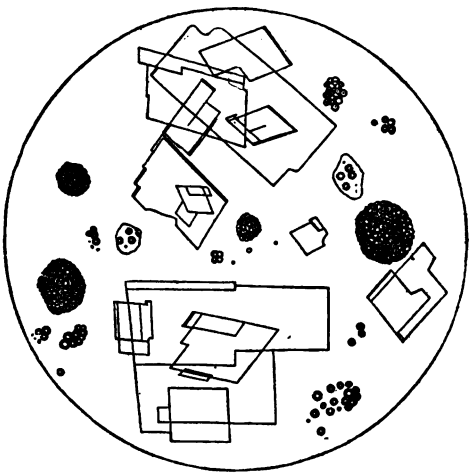


FIG. 8. Crystals of Cholesterine and Fatty Aggregations. (Roberts.)

Under the microscope, leucine appears as more or less yellow-colored, refracting spheres of various sizes, which here and there show a disposition to aggregate, and, where the edges of two spheres come in contact, to fuse. They bear a strong resemblance to oil drops, but are distinguished from them by their less strongly refracting border and insolubility in ether. Furthermore, when observed

under suitable illumination, crystals of leucine exhibit in their interior a crystalline structure.

Crystals of ammonium urate may resemble leucine spheres, but upon the application of heat the

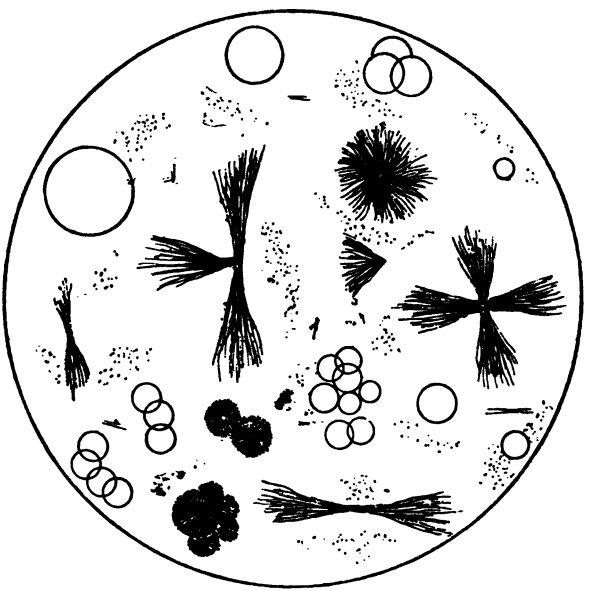


FIG. 9. Leucine Spheres and Tyrosine Needles.

former disappear. More frequently the urate of ammonium crystal is recognized by the spicules on its surface.

Tyrosine crystallizes in delicate silky needles, ranged in tufts or sheaf-like aggregations, which

occasionally cross each other at their middle constricted portions.

### Bilirubin (Hæmatoidin).

Crystals of hæmatoidin are found in old blood extravasations and blood clots. Whenever any communication exists between such extravasations or clots and the urine, the hæmatoidin crystals may appear in the sediment. Under the microscope they appear as transparent ruby-red rhombic flakes, or as delicate needles varying in color from yellow to yellowish brown.

*Chemical Characters.* — Hæmatoidin contains no iron; is soluble in chloroform, but insoluble in water, alcohol, ether, and acetic acid.

## Organized Sediment.

### Mucus.

Normal urine always contains a small amount of mucus and epithelium. The former is a normal secretion of the mucous membrane lining the urinary passages, and is therefore washed out by the flow of the urine; the latter, as a result of the normal wear and tear to which the tissues are subjected, becomes loosened, and is also carried away by the urine. It is therefore a mistake to speak of urine as containing *no* sediment. Irrita-

tion or inflammation increases both these constituents, and by identifying the kind of epithelium which is present in excess, the seat of the inflammatory process may be determined. Simple irritation, however, such as may occur from a concentrated urine, increases at times only the mucus, which, since it is so transparent and similar to urine in its index of refraction, is recognized often only by other than its optical properties.

By the action of acetic acid, mucin, which is a constituent of mucus, is separated as delicate fibrillated bands, which at times are tortuous in outline and at other times appear as delicate threads.

These mucus coagula often appear in urine to which no acid has been added, and in such instances are due to the action of acids developed in the course of the acid fermentation.

Under the microscope these coagula appear as threads with pointed extremities and varying irregularly in their diameter, whereas hyaline casts, with which they may be confounded, have a uniform diameter, increasing or diminishing symmetrically, and are usually rounded at the ends (Fig. 10).

At times leucocytes, epithelium, and crystalline salts attach themselves to or become embedded in mucus, whereby it becomes more distinctly visible.

When, as a result of irritation, the amount of mucus is largely increased, the urine becomes more

or less viscid, and is designated "ropy." In addition, cells from the seat of irritation are embedded in the mucus cloud, as stated above.

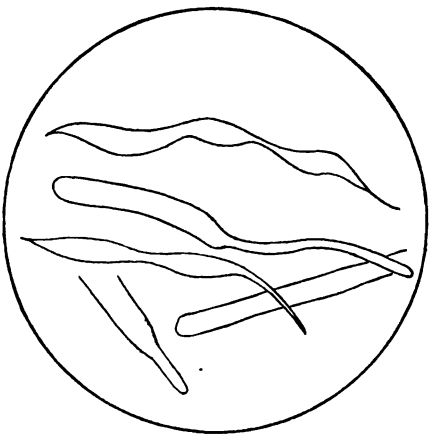


FIG. 10. Mucus Coagula and Hyaline Casts.

## LEUCOCYTES AND PUS.

Mucus is rarely present in any considerable quantity without being accompanied by more or less pus, as the causes which produce both differ simply in degree. Pus, however, contains albumen, whereas mucus does not. Therefore, in a general way, it may be stated that the absence of albumen from a urine containing mucus is presumptive evidence that pus is absent as well.

The presence of pus is determined microscopically by detection of the pus corpuscle in the sediment. Anatomically and in appearance the pus corpuscle and leucocyte (white corpuscle of the blood) are identical. It is customary, however, to use these terms with a quantitative significance. When only a few scattered corpuscles are present they are termed leucocytes, when present in large numbers they are called pus corpuscles. The pus corpuscle, as it appears in urine, is a small, granular, more or less spherical cell, rather larger than a blood disk (i. e. about 10 $\mu$ in diameter), and containing one or more nuclei. It thus resembles very closely the round epithelial cells; but the latter contain only one nucleus, which is quite distinct, whereas the pus corpuscle may contain several, which, however, are not always easily discernible until acetic acid has been added. If a few drops of the acid be allowed to flow under the cover-glass upon pus corpuscles, they swell, are freed of their granular contents, and the nucleus or nuclei come out with great distinctness. Pus from the seat of an old inflammation often exhibits, when acted upon by acetic acid, a characteristic nucleus of horse-

FIG. 11. Mucus and Pus Corpuscles, before and after the addition of acetic acid. (Tyson.)

shoe shape. It probably represents the fusion of several nuclei.

Caustic alkalies have a characteristic and pronounced action upon pus. They destroy its morphological identity, and convert it into a viscid gelatinous mass. To this fact is due the "ropy" character which alkaline urine, containing pus in considerable quantity, assumes. Upon the same fact is based the test of Donné, whereby the presence of pus in urine which is still acid is established. After settling, the deposit in which pus is suspected is separated by decantation from the supernatant urine. If pus is present, this deposit is converted, by the addition of ammonic or sodic hydrate, into a cohesive gelatinous lump.

The commonest sources of pus in the urine are inflammations of the renal pelvis, bladder, prostate, and urethra. In each instance, except cystitis, the urine is usually acid, and the presence of pus is determined by Donné's test. As a result of the ammoniacal changes incident to cystitis, the urine may become "ropy" while yet within the bladder, and so plug the urethra as to cause all the distressing symptoms of obstructive anuria. (*Vide* page 134.)

The presence of pus often clears up a doubt concerning the identity of bladder or vaginal cells, for pus is associated most frequently with the former,

although purulent and leucorrhœal discharges from the vagina may lead to the presence of vaginal cells and pus in the urine.

The association of mucus and pus together with cells from the seat of irritation renders it important to determine next the characters by which the genito-urinary epithelium may be identified.

### The Epithelium.

To describe the epithelium which may appear in the urine, it is necessary to have a unit of reference, and in addition, for the purpose of mensuration, an element which is both familiar and tolerably constant in size. The bladder cell has been adopted as the former, and the pus corpuscle as the latter.

The epithelium of the *bladder* is composed of the largest cells found in the urinary passages. They are flat or plate-like, irregularly polygonal in outline, three or four times the diameter of a pus corpuscle, and contain a single nucleus.

When present in excess, many of the bladder cells are in single layers and adherent by their edges. This serves to differentiate them from vaginal cells, which they resemble. Besides being on the average somewhat larger, vaginal cells, when aggregated in masses, appear upon careful focusing to be made up of several distinct and overlapping

layers. Moreover, it is somewhat difficult to distinguish the individual vaginal cells.

From the bladder, both toward the external meatus and the kidney, the individual cells of the successive tissues progressively diminish in size.

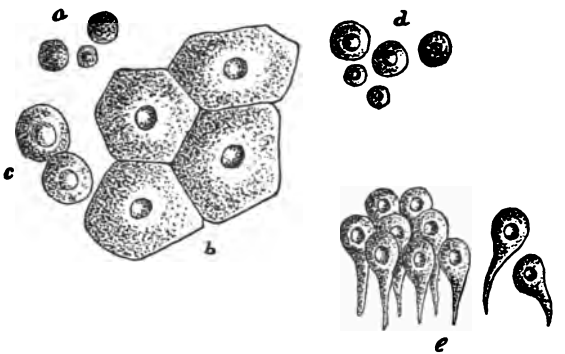



FIG. 12. Varieties of Epithelium.

*a*. Two Leucocytes and a Blood Globule.
*b*. Bladder Cells.
*c*. Cells from Neck of Bladder and Prostate.
*d*. Large and small *Renal* Cells; the one at the right contains fat drops.
*e*. Cordate Cells from the Renal Pelvis.

The cells of the *ureters* are seldom met with in the sediment, and are of no great importance. Inflammatory processes, whether extending upwards from the bladder, or downwards from the renal pelvis, apparently skip the ureters. Occasionally, however, as the result of the passage of a

calculus, the ureter cells are torn away and appear in the sediment. They are nucleated spindle-shaped cells.

Cells from the *pelvis of the kidney*, according as they come from its superficial or deeper epithelial layers, are of two forms, — cordate and round. In acute inflammation of the pelvis the superficial layers are first detached, and are present in the sediment in excess. The individual cell has a cordate or battle-door outline, the head of which is about as large as a pus corpuscle, and contains the nucleus. Although somewhat unusual, they may appear in groups, the cells overlapping each other like shingles on a roof. This condition is more common when the inflammatory process has extended down from the kidney.

After a few days of active inflammation, the cells of the deeper layers are detached. In size, shape, and appearance, they are like a renal cell, from which they cannot be distinguished. If from the pelvis, however, there is usually present in addition some blood and an excess of pus corpuscles, which are recognized by their multinuclear structure.

The cells from the *kidney* are, as just stated, like those from the pelvis, but they vary more in size. If from the smaller renal tubules they are slightly smaller, and if from the larger tubules

they are somewhat larger, than a pus corpuscle. In addition, if the cells are of renal origin there are always present casts to which similar cells are attached, or in which they are embedded. At times the renal cells contain fat drops.

In advanced stages of chronic parenchymatous nephritis, many of the renal cells undergo complete fatty degeneration, and appear in the sediment as more or less spherical aggregations of small fat drops. To these the name of *compound granule cells* has been given. (*Vide* Fig. 14, page 117.)

The cells from the *neck of the bladder* and the *prostatic urethra* (male) resemble those of the bladder proper. They are, however, smaller, denser, and generally rounder than the bladder cell. Similar cells occur in the female urethra, and are found in female urine under normal conditions.

*Below the prostate*, the cells are still smaller, both round and cordate, resembling those of the renal pelvis. If it is necessary to determine whether they are from the urethra (gonorrhœa, etc.), it is to be remarked that, when the urethra is inflamed independently of the bladder, the urine is cloudy at the beginning of micturition, and shortly becomes clear. In addition, there are present an excess of pus and more or less blood, while the cells are embedded in shreds of mucus, viz. gonorrhœal threads.

## Blood Disks.

The causes and general characters of the urine which suggest the presence of blood have already been discussed, and it now remains only to indicate the appearances by which these suggestions are confirmed; viz. by recognizing the optical characters, as viewed under the microscope, of

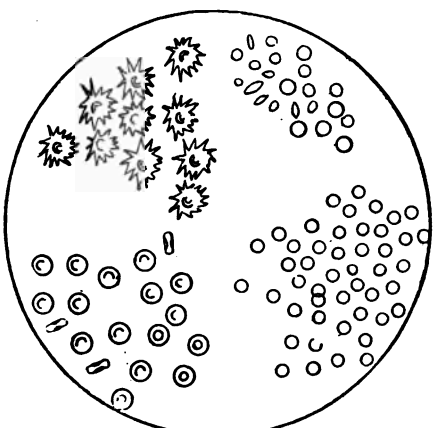


Fig. 13. Blood Disks. Those in the left half of the circle are *normal*, — those in the upper quadrant being crenated. Those in the right half are *abnormal*.

the disks themselves. These differ according to the place at which they enter the urine, and the length of time that they remain in it.

The disks that enter the urine below the kidneys, and have therefore remained in the urine

only a relatively short time, present a tolerably *normal* appearance. They are circular, biconcave disks of about one half the diameter of a pus corpuscle, and of a slightly yellow color. Their biconcave structure is proved by the alternation of light and shadow at the centre and periphery as the objective-glass of the microscope is approximated to them. When seen on edge, the disks resemble a dumb-bell, and their biconcave structure becomes more evident. If the urine is a concentrated one, the disks shrink, and together with their diminution in size exhibit a crenated or irregular outline. They are still to be regarded as normal globules.

When poured into the urine before it leaves the kidney, the disks undergo changes by which they lose their color and biconcave structure, diminish one half in size and become spherical, looking very much like a small, round ring. The disk in which these changes have occurred is to be regarded as *abnormal.* The same alterations occur in dilute ammoniacal urine, but with the increase of alkalinity the globules slowly disintegrate and are finally dissolved.

### Fibrin.

Associated with blood, fibrin coagula may occasionally be found. These coagula are usually

colored by the action of blood pigment, and exhibit a vacuolar appearance, i. e looking as though something had been shaken out of their interior.

### Renal Casts.

The identification of renal casts is a most important step in the diagnosis of renal disease. They are, as their name implies, casts or moulds of the uriniferous tubules, produced by the presence in the latter of some coagulable matter. This material, as it sets, entangles in its substance whatever débris is present in the tubules at the time, and, subsequently contracting a little, is washed out of the tubules into the renal pelvis, and thence to the bladder and urine receptacle.

In general, true albuminuria is presumptive evidence of the presence of casts. There have been only a few isolated cases in which casts have been detected unaccompanied by albuminuria.

Several theories as to the origin of casts exist. It goes without saying that in cases of renal hemorrhage the blood may clot in the tubules and give rise to a fibrin cast. Three other theories of some importance, however, are to be entertained.

1. *The Transudation into the Tubules of some Coagulable Material, probably Albuminous, from the Blood.* — If the renal vein of a normal kidney be tied, there results an œdema of the organ. If

it then be put into boiling water and sections examined, a homogeneous glistening material, which is chemically a fixed albuminate, will be observed in the lymph spaces and interstitial tissue.

2. *An Abnormal Product of Epithelial Secretion or Activity.* — Similar suppositions are entertained with regard to the processes observed in many cases of thyroid goitre.

3. *A Product or Result of Cell Degeneration.* — In fresh sections of the kidney filled with casts, the material of which the latter are composed exhibits shadowy outlines suggestive of cellular origin. Hence it is possible to regard this coagulated material as composed of disintegrating or wholly disintegrated cells, i. e. a kind of hyaline degeneration.

Whatever its origin may be, this homogeneous albuminoid material differs at times in its optical characters. It may be highly refractile, granular, and colored, or it may be perfectly clear, colorless, and of a refrangibility differing but slightly from that of the urine itself.

It is perfectly obvious that, in the process of setting, any loose material, e. g. epithelium, blood disks, granular débris, etc., present in the tubules, is liable to become adherent to or embedded in the setting mass, and thus alter the appearance of the cast. Upon the changes so effected a classification

of casts is based, although it is to be remembered that all casts, except perhaps the fibrin casts mentioned above, are at base hyaline.

- **Casts.**
  - 1. Hyaline,
    - pure.
    - fibrinous.
    - waxy.
  - 2. Epithelial.
  - 3. Blood.
  - 4. Fatty
  - 5. Granular,
    - colorless
      - fine.
      - coarse.
    - brown
      - fine.
      - coarse.
  - 6. Crystalline,
    - uric acid and urates.
    - calcic oxalate.
  - 7. Pus.

In general, casts are recognized when viewed under the microscope by their more or less uniformly cylindrical appearance and rounded ends. Their length is usually greater, and often several times greater, than their width. If their diameter diminishes, it is usually at one point (*cf.* Mucous Casts, page 105).

At times casts have a divergent branch, i. e. Y-shaped, indicating their origin at some point where the second convoluted portion of the tubules enters the collecting or straight tubules. It is inconceivable how casts formed behind the narrowed descending loop of Henle, i. e. in the first convoluted portions, can be eliminated as formed in the urine.

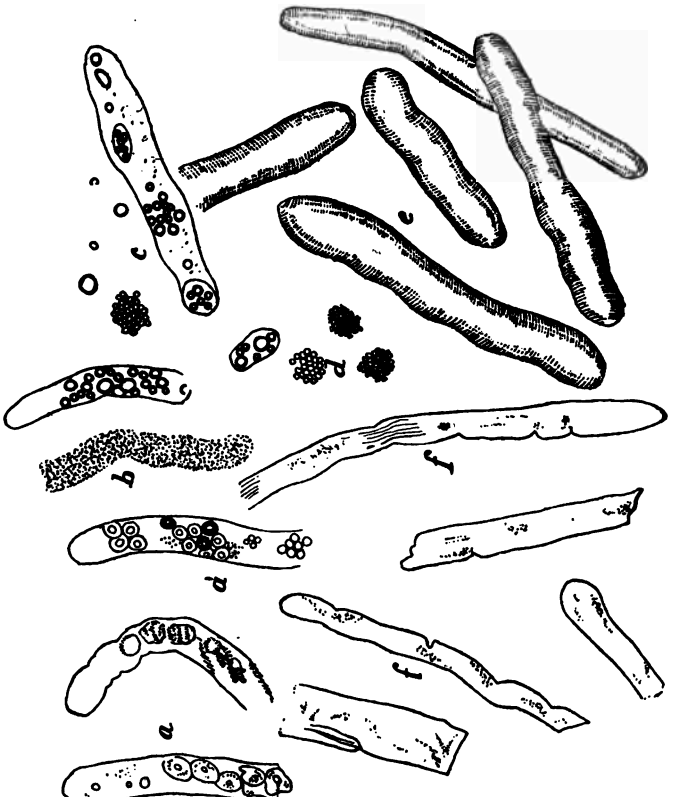



FIG. 14. Varieties of Renal Casts.

*a*. Epithelial, — *a'* containing at its lower end a group of abnormal Blood Globules.
*b*. Fine Granular.
*c*. Fatty.
*d*. Compound Granule Cells.
*e*. Waxy.
*f*, *f*. Pure Hyaline.

*Hyaline Casts.* — In the broad sense, hyaline means a clear homogeneous cast. This would include the waxy and fibrinous casts, presently to be described; hence it is better to use the prefix *pure*, as it restricts the term to those casts which are clear, homogeneous, and of slight refrangibility. They are often seen with difficulty, and may be overlooked unless the illumination of the field be modified by shading with the hand or by manipulation of the mirror itself.

A *waxy cast* is in no way different from a pure hyaline, save that its diameter may be somewhat greater and its refrangibility much increased. It looks more solid, and not unlike molten wax. In fact, it bears somewhat the same relation to a hyaline cast that a fat drop does to an abnormal blood disk.

A *fibrinous cast* is like the waxy, save that it is colored by blood pigment, usually, a yellow or yellowish brown. This form is usually accompanied by isolated blood globules in the sediment. Its composition is not definitely known. It does not necessarily follow, however, that they are composed of fibrin. The name is probably a misnomer.

The other casts are simply hyaline, with which different formed elements have become united; viz. *epithelial*, when holding renal cells; *blood*, when

blood disks are present; *fatty*, when containing fat drops; and *granular*, when containing granular débris.

According to the color or absence of color, granular casts may be brown or colorless; according to the size of the granules, fine, medium, or coarse; and according to the quantity, highly, moderately, or slightly granular. Brown granular casts are made up of disintegrated urates, blood globules, and epithelium, colored by blood pigment. The source and nature of the materials composing the coarse granular casts is as yet doubtful. They are commonly associated with waxy casts.

*Mixed casts* are, as the name implies, those in which the different formed elements are associated in one cast.

*Crystalline casts* are those in which the crystalline matter, separating in the tubules, has been caught in the coagulating material. Such crystals are the urates, uric acid, and calcic oxalate.

*Pus casts* may occur in the course of acute inflammatory conditions. In pyelitis and pyelonephritis the pus corpuscles are frequently agglomerated in masses which are suggestive of casts and may come from the straight tubules. They are usually of considerable size, — much larger than the renal casts.

Casts of the seminal tubules may appear, and

are recognized by the associated presence of spermatozoa.

*Hints on the Examination for Casts.*— Owing to their extreme lightness, casts settle slowly. The urine should be collected in a urine-glass (i. e. a more or less conical glass, having a rounded bottom and holding about a pint), covered with a glass plate and allowed to stand some twelve hours. To obtain a specimen, a pipette, made of glass tubing more than sufficiently long to reach the bottom, and drawn nearly to a point at one end, is used. With the fore-finger pressed firmly over the smooth proximal end, the pointed end is passed down to the sediment, which is seen in a mass at the bottom or on the sides of the glass near the bottom. Having selected a spot for trial, the fore-finger is raised an instant; a *little* of the sediment rises up into the pipette, and the finger is clapped down again. The pipette is then carefully and slowly withdrawn, and while the finger is still pressed on the end, the point is wiped with a soft linen cloth. The sediment in the point of the pipette is then placed on a glass slide by raising the fore-finger, and examined under the microscope, using a tolerably high power (Zeiss Oc. 3, Obj. D).

In case there is considerable sediment it is always well to take specimens from different layers, — top, middle, and bottom, — and never to feel

satisfied with the examination of one specimen, unless a positive result is obtained. When there is a very slight sediment, it often attaches itself as a delicate film to the sides of the glass near the bottom. Specimens from this should be examined, first loosening, by scratching it, with the point of the pipette, and then collecting in the usual way. Success will often attend this procedure.

### Fat.

The appearances and significance of fat in the urine have already been sufficiently treated (*vide* page 73).

### Spermatozoa.

There are no characters imparted to the urine by spermatozoa which are perfectly characteristic of their presence. When present in abundance, they may form a delicate flocculent cloud in the urine, which under the microscope is resolved into a mass of spermatozoa embedded in a fine granular menstruum. The microscopic appearances of spermatozoa, with their flattened pyriform body and long filamentous tail, are sufficiently well known, and require no further description.

They occur in the urine of males suffering from spermatorrhœa, and after coitus, nocturnal emissions, etc.; in the urine of females, after coitus or

attempted coitus. The recognition of spermatozoa in the latter instance may be a matter of considerable medico-legal importance, i. e. cases of suspected rape. With the exception of such cases, the examination of the sediment for spermatozoa is of little or no importance. It is to be remarked in this connection, however, that the spermatozoa resist disintegration to a remarkable degree, and may be discovered in the urine entire for several days after its elimination.

Albumen is a constituent of the seminal fluid; therefore, when the latter is present to any considerable extent in the urine, it is possible to get tests for albumen. It is sufficient simply to warn against such a source of error.

### Fungi.

The fungi which may be found in urinary sediments consist of the saccharomyces, sarcinæ, and bacteria.

*Saccharomyces.* — *Pencilium glaucum* (or acid fermentation spore, as it is called by many who believe that it plays a part in the changes of that stage) is found in acid urine as small oval spores united in chains which branch here and there, forming characteristic thalli. Growth is by budding. Practically, the importance of the Pencilium is the liability of the observer to confound

it with the oval form of calcic oxalate, abnormal blood disks, and the sugar spore. Calcic oxalate crystals do not unite in chains, and are biconcave in appearance. The blood globule, although of about the same size, is not oval, and gives no evidence of budding. The sugar spore is larger.

*Torulæ cerevisiæ*, or sugar spores, are found in saccharine urine, or in urine which has been standing in a vessel that previously contained sugar. In appearance they differ from the Pencilium only by the increased size of the individual spore, which is half as large again.

The *sarcina* of vomitus has been encountered in the sediment a few times. It is composed of numerous spores arranged in cubes, four deep (or some multiple of four). Many attempts have failed to show that the form met with in the urine is an independent smaller variety originating in the bladder. It is probable, therefore, that when present in the urine the sarcina is extraneous, and not indicative of a pathological process.

A great variety of *bacteria* may be found in urine, especially after it has undergone decomposition. There is reason to believe that at times bacteria exist in the urine when passed, but in the great majority of instances these organisms gain access only after the urine has been exposed to the air. The alkaline fermentation of the urine

is believed by many to be due to the decomposition of urea by the action of a micrococcus which Cohn has called M. Ureæ. It is probable that this organism is often introduced into the bladder by the passage of unclean catheters and sounds, the result of which is a bacterial fermentation inside the bladder, and the conversion of the urea to ammonic carbonate. The innocuous acid urine thereby becomes changed to a fiery alkaline irritant, which may by its action upon the urinary tissues induce serious consequences, and even death.

Other forms, such as the rod, vibrio, and leptothrix, may be encountered, either singly or massed together as zoöglœa.

When present in quantity, bacteria impart a cloudiness to the urine which, inasmuch as they pass the pores of the filter-paper, is not wholly removed by filtration. When present together with considerable mucus, the pores of the filter-paper become more or less plugged, and the urine is only difficultly filterable. Under such circumstances the precipitation of the earthy or (if urine is already alkaline) alkaline phosphates will carry down the bacteria and mucus, after which the urine may be filtered with ease.

In this connection it may be said that the *Bacillus tuberculosis* has occasionally been detected

in the urine. When found, a considerable quantity of pus and disintegrated tissue is usually present as well.

To detect the bacilli, allow the urine to stand for a short time, and place a little of the pus between two cover-glasses. Dry each carefully, and stain like ordinary phthisical sputum.

### Morbid Growths.

Cancer cells, or other evidences of morbid growths, are very seldom met with in the sediment, for they do not pass out with the urine unless mechanically dislodged by a catheter or other instrument. Even then they can be differentiated from the normal cells of the urinary passages only with the greatest difficulty. In short, no proof of neoplasm can be expected by an examination of the sediment.

### Entozoa.

The hooklets as well as the cysts of the *echinococcus* have been discovered a few times in the urine; also the vermiform parasite *Filaria sanguinis hominis*, with which chyluria is associated. Neither is common in this climate. Other entozoa are too rare to be mentioned.

### Extraneous Matter.

This class includes a great variety of substances which may be met with in the examination of the sediment, and with which every student should familiarize himself. Among such are fibres of cotton, woollen, and linen; human hair, cat's hair, splinters of wood, oil globules, air bubbles, and starch granules. Finally, if the slide be not thoroughly cleaned, the remains of a previous examination, or scratches and marks on the slide, may mislead, or at least perplex, the beginner.

### To preserve Urinary Sediments for Subsequent Examination.

Crystalline sediments are preserved only with difficulty, and inasmuch as they are so readily obtainable, there is no advantage in attempting their preservation. Organized sediment, on the other hand, may best be preserved in a filtered solution of acetate of potassium, to which a little phenol or salicylic acid has been added. The urine is separated from the sediment by decantation, and replaced by the potassium acetate solution after a few decantations with it.

## CHAPTER IV.

### URINARY CONCRETIONS.

URINARY concretions are hard, mineral-like bodies of varying size. They are at times voided in the urine, or, if too large to pass the urinary ducts, become lodged in some portion of the urinary passages. In the latter case they may be situated at any point whatever, from the kidney tubules to the meatus; in fact, they may be so fused as to form a more or less continuous stony cast of the whole urinary tract.

They are limited in size only by the dimensions of the cavity or passage in which they lie. This property of size forms a ready basis for their classification, and concretions are therefore divided into sand, gravel, and calculi.

*Sand* usually consists of small crystals, which are seen clearly only by the aid of a lens of low power.

*Gravel* consists of larger crystals, which are easily seen with the unaided eye, and of such a size that they pass the urethra without difficulty. The continual rubbing of the gravel particles on each other frequently results in "facetting" many of them.

*Calculi* are concretions which are too large to be spontaneously voided.

The color of a concretion varies according to its composition, and whether it has been acted upon by blood pigment, — white, yellow, or brown.

The *rationale* of concretion formation is very simple. Any change occurring in the urine, while yet within the body, whereby the soluble constituents become insoluble, is followed by a separation of those substances, either in a crystalline or amorphous condition. The irritation of the epithelium, induced by the passage of the insoluble matter, causes an increased secretion of mucus, by which the precipitated matter becomes agglutinated, and the masses thus formed serve as nuclei of future calculi.

It has already been shown, in speaking of the processes of urine fermentation, how the various non-organized constituents of the urine are rendered insoluble. It follows, therefore, that the same causes which bring about those changes are equally causative of concretions and calculi; viz. increased acidity of the urine, however induced, is followed by a separation of the acid urates and uric acid, and increased alkalinity by the precipitation of the earthy phosphates (amorphous when precipitated by fixed hydrates, crystalline when due to fermentative processes). Any increased formation, as following upon defective oxidation of the less soluble normal

or abnormal constituents, and finally the presence in the passages of foreign particles (bit of catheter, wood, etc. in the bladder) may be a cause of calculus. The presence of any foreign body (including a calculus) in the bladder excites an inflammation of that viscus, which results at the time in an alkaline urine with a deposition of the phosphates, and later in hypertrophy, dilatation, and ulceration of the bladder walls, with the consequences arising therefrom. It is due to these spontaneous changes that a distinction has arisen between primary and secondary portions of a calculus. Those portions which are first to form are accordingly called *primary*, while those which are formed as a result of the changes induced by the presence of the primary portions are called *secondary*.

The constituents of the primary and secondary portions are tabulated as follows: —

| PRIMARY. | SECONDARY. |
|---|---|
| Uric acid. | Urate of ammonium. |
| Urates. | Earthy phosphates. |
| Calcic oxalate. | Calcic carbonate. |
| Calcic phosphate. } Not common in | |
| Calcic carbonate. } human urine. | |
| Cystine. | |
| Xanthine. | |
| Indigo. | |
| Urostealith. | |
| Silica. | |
| Bilirubin. | |
| Blood-clot. | |
| Albuminous substances. | |
| Foreign bodies introduced into the bladder. | |

In connection with the above distinctions, a calculus is also divided into a *nucleus*, *body*, and *crust*. The nucleus and body usually consist of the primary constituents, while the crust is deposited as a result of the alkaline changes of the urine, and therefore consists of secondary portions.

The surface of a calculus may be smooth or rough. Smooth calculi always attain a larger size than rough; hence calculi of uric acid and phosphates are frequently of considerable size. Calculi of calcic oxalate always have a rough surface, and on that account are often called *mulberry calculi*. They are productive of greater irritation, and induce secondary changes sooner than the smoother and hence less irritating varieties.

A calculus grows by the deposition of successive layers about the nucleus. This frequently occurs irregularly, as shown by the position of the nucleus, which may be either at the centre or at some point nearer the periphery.

Calculi are not always of simple composition, but oftener *compound*, i. e. composed of different constituents, which are frequently arranged in concentric lamellæ. Thus a history of the growth of the calculus may be obtained by an analysis of its different layers.

The number of calculi varies. As many as one hundred have been counted in one cavity. In such

cases the rubbing of one calculus on another may give rise to many modifications in shape, — round, oval, irregularly oval, facetted, etc. Sometimes two nuclei become united, and subsequently covered with a secondary deposit.

*The Examination of a Calculus.* — The calculus is first sawed in two, and with a penknife a little of each layer in succession is scraped off into a watch-glass and examined.

The first step is to determine the presence of uric acid, and the second, whether it is free or combined as urates. The following scheme may be useful as a guide to the determination of the ordinary constituents of calculi.

### ANALYSIS OF URINARY CALCULI.

#### (1.) Preliminary Examination.

Heat scrapings on platinum : —

Albumen = flame $\bar{c}$ odor of burnt horn.

Uriostealith = flame $\bar{c}$ odor of shellac and benzoin.

Cystine = flame blue, odor of $SO_2$.

Xanthine and Uric Acid = no flame, — char.

Alk. Urates = alk. residue sol. in $H_2O$.

Earthy Phosphates = residue sol. in $H\bar{A}$ $\bar{s}$ effervescence.

$Ca\bar{O} + CaCO_3$ = residue sol. in $H\bar{A}$ $\bar{c}$ effervescence.

$CaCO_3$ — original powder sol. in $H\bar{A}$ $\bar{c}$ effervescence.

$Ca\bar{O}$ — original powder insol. in $H\bar{A}$.

Silica = residue insol. in HCl.

Murexide Test for $H_2\bar{U}$ : —

$HNO_3$ + evap. = pink residue + $NH_4OH$ = purple color = Uric Acid and Urates.

$HNO_3$ + evap. + KOH = violet disappears on heat, if $H_2\bar{U}$. Violet increases on heat, if Xanthine.

(2.) SYSTEMATIC EXAMINATION.

Presence of uric acid shown by (1). Boil scrapings in $H_2O$ and filter.

A. Filtrate + HCl. Let stand 24° = crystals $H_2\bar{U}$.

Bases in sol. Concentrate.

$Ca\bar{U}$ = 1 gtt + $(NH_4)_2\bar{O}$ = cryst. $Ca\bar{O}$.

$Mg\bar{U}$ = 1 gtt + $NH_4OH$ + $Na_2HPO_4$ = cryst. $MgNH_4PO_4$.

$Na_2U$ = 1 gtt + $PtCl_4$ = after conc. prisms, $Na_2PtCl_6$.

$K_2\bar{U}$ and $(NH_4)_2\bar{U}$ = 1 gtt + $PtCl_4$ = Dodecahedra, $\begin{cases} K_2PtCl_6. \\ (NH_4)_2PtCl_6. \end{cases}$

$K_2\bar{U}$ evap. and ignite on mica. Res. + HCl + $PtCl_4$ = $K_2PtCl_6$.

$(NH_4)_2U$ evap. and ignite, no cryst. c̄ $PtCl_4$.

B. Portion insol. in $H_2O$ + HCl.

$H_2\bar{U}$ = insol.

$CaCO_3$ = sol. c̄ effervescence. Filter + $NH_4OH$ = ppt.

$Ca\bar{O}$, $Ca_3(PO_4)_2$ and $MgNH_4PO_4$.

Wash $Ca\bar{O}$ insol. in $H\bar{A}$ Filter + $(NH_4)_2\bar{O}$ to filtrate.

$Ca_3(PO_4)_2$ gives ppt of CaO. Filter + $NH_4OH$ to filtrate = ppt $MgNH_4PO_4$.

## CHAPTER V.

### THE URINE AS AFFECTED BY GENERAL DISEASES.

THE urinary excretion bears an intimate relation to the various metabolic processes. This is shown by the fact, that, in many constitutional diseases, modifications of the excretion are so constant that a systematic examination of the urine becomes at times of decided value in diagnosis.

In the first place, variation in the quantity of urine passed, e. g. such symptoms as polyuria, oliguria, and anuria, is characteristic of several general affections, as follows.

Polyuria, or the passage of a large amount of urine, is characteristic of the two forms of diabetes and hydruria, whose specific characters have already been stated (*vide* page 13). In addition, it may be said that, aside from excessive drinking, hydruria is frequently the result of severe mental disturbances, e. g. great anxiety, grief, nervousness, etc., or of apoplectic hemorrhages. In the latter instance, the increased flow begins about half an hour after the attack, and in severe cases there may be an associated albuminuria and glycosuria.

Such cases warrant a grave prognosis. Ordinary hydruria ceases in a few days.

Polyuria is also usual in convalescence from most acute diseases, and quite characteristic of certain forms of renal disease.

Oliguria, or diminished urine, characterizes the active stage of most acute febrile processes, and many chronic diseases. In fact, slight oliguria occurs in all chronic diseases except the two forms of diabetes.

It is a matter of some consequence to the healthy individual if he persistently fails to pass a full litre of urine daily. The urine becomes concentrated, and, aside from acting as an irritant to the renal tissues, there is also danger of developing a calculus diathesis, i. e. a tendency to the separation, in the urinary tract, of the less soluble constituents of the urine. This tendency can in most cases be corrected by drinking more water.

Anuria, or suppression of the urine, is a serious condition, and arises from two general causes: —

1. A mechanical obstruction to the flow, situated somewhere between the meatus and renal pelves. Most frequently this form is due to the impaction of a stone in the ureter of a person having (*a*) but a single functional kidney, or (*b*) some malformation whereby only one ureter exists. It occurs next in order of frequency as a result of the destruc-

tion or stenosis of the terminal ends of the ureters by morbid growths at the base of the bladder. Of course oliguria precedes the anuria in such cases. Finally, stenosis anywhere in the course of the urethra, the impaction of calculi in the urethra, or the obstruction (by bits of neoplasm, ropy urine, etc.) of the urethra at its point of union with the bladder, may give rise to a temporary anuria.

In unrelieved cases, retention, dilatation of the channels behind the point of obstruction, hydronephrosis, and cystic dilatation of the kidneys ensue, culminating in uræmic convulsions and death. Such cases of anuria are to be considered as *obstructive.*

The urine, for it is rare that a little is not voided before death occurs, is pale, at times slightly tinged with blood, watery, and of very low specific gravity.

2. Organic disease of the renal tissue, whereby it is no longer able to separate the urine from the blood. This condition obtains just before the fatal termination of renal diseases. In this class are to be included also those cases which are apparently due to some disturbance of innervation, whereby the separation of the urine is temporarily suspended. Such forms of anuria are met with in severe poisoning by turpentine and other irritants, in states of collapse or shock, after catheterization, etc. They form a group quite opposed to the

former in cause, duration, and termination, and may be considered as *non-obstructive.*

The urine of these cases is high-colored, concentrated, albuminous, and contains casts.

Cases of non-obstructive anuria are seldom fatal, last only a day or two, and are in most cases easily relieved. Cases of obstructive anuria are nearly always fatal, run a longer course, a week or ten days, and are beyond means of relief.

After the above, the modifications of the urine to be observed are those which are dependent on the nature of the process, viz. whether febrile or not, and, in the same connection, whether acute or chronic.

Fever urine is diminished in amount, high-colored, of increased acidity and specific gravity, and contains considerable sediment. As a result of the concentration, the total solids are relatively and in some cases absolutely increased. Urea and uric acid are both increased, and in the same proportion; but in those cases in which respiration is hindered, uric acid is increased in a greater proportion than urea. If the case is about to terminate fatally, the amount of urea decreases. If the temperature is high, there may be albuminuria. If the fever is accompanied by any considerable exudation, e. g. pneumonia, peritonitis, etc., the chlorides disappear from the urine. In ordinary

febrile conditions the absolute amount of chlorides is diminished; but, owing to the diminished quantity of urine, they may be relatively normal. Absorption of the exudation is followed by the reappearance or increase of the chlorides.

With convalescence, the concentration of the urine gradually disappears, the reaction becomes more nearly neutral, the specific gravity falls, and the amount increases. The increase may considerably exceed the normal (2000 c. c.), but as health is re-established the quantity again diminishes, and becomes settled at the normal point.

The urine of intermittent fever is an exception to the ordinary rule. In this affection, the urine is usually normal on the day of the paroxysm, and exhibits febrile characters the day after.

By an examination of the urine alone, no difference can be determined between the febrile urine and that due to simple, non-febrile concentration.

Besides these general characters, the urines of acute febrile diseases are often peculiar in some special way, as follows.

In peritonitis the chlorides are frequently absent, and the indoxyl much increased.

In rheumatic fever the chlorides follow the general rule, and the phosphates are usually increased. If the rheumatism becomes complicated with pericarditis, the chlorides and earthy phosphates will disappear.

The differential diagnosis between typhoid fever and meningitis is often extremely difficult, but may at times be greatly facilitated by a careful consideration of the urine, viz.: —

| Typhoid Fever. | Meningitis. |
|---|---|
| In early stage excessively acid. | Only slightly acid at first. |
| Sp. gr only slightly increased. | Sp. gr. considerably increased. |
| Chlorides normal or slightly diminished. | Chlorides much diminished. |
| Phosphates diminished. | Phosphates much increased. Boiling of urine in a test tube is sufficient to precipitate the phosphates. |

Of late, the so-called *diazo-reaction* has been used to confirm the existence of the typhoidal state. This reaction, however, is not observed in all cases of undoubted typhoid, and it does occur in other affections, viz. tuberculosis, measles (desquamative stage), and in albuminous urines associated with extreme pyrexia. The reaction may be obtained from the urine at about the end of the first week, and coincident in time with the appearance of rose-spots on the body.

Two solutions are required: —

Solution A.

| | | |
|---|---|---|
| Hydrochloric acid | ♏ 72, | or 1 part. |
| Sulphanilic acid | gr. 10, | or to saturation. |
| Distilled water | ʒ 3, | or 20 parts. |

SOLUTION B.

¼% solution (freshly prepared) Sodic Nitrite in distilled water.

To perform the test: —

In a test tube put of Sol. A 25 parts.
Sol. B 1 part.
Urine 26 parts.
Ammonic Hydrate to alkalinity.

Positive result = an immediate brilliant crimson red color and a greenish yellow precipitate in 24°.

Acute yellow atrophy of the liver, typhus fever, small-pox, and poisoning by arseniuretted hydrogen and phosphorus, are not characterized by an increase, but on the other hand by a great diminution, if not entire absence, of urea. As a result of the morbid processes, complete oxidation of the nitrogenous tissues does not occur, and in the place of urea and uric acid, leucine and tyrosine are excreted. Albuminuria and hæmoglobinuria are also observed in these cases.

Acute intestinal diseases are accompanied by an increase of indoxyl (e. g. 98 milligrams), but only in case it is the small intestine that is affected.

During the acute stage of cholera, the amount of urine, as well as of urea, is diminished. Much of the latter is eliminated in the sweat and fæces. Indoxyl, however, is increased. During convalescence the urea and amount of urine increase in about the same proportion.

In yellow-fever the urea is not so much increased as in ordinary cases of fever.

The urine of *chronic disease* exhibits characters incident to the decreased metabolic activity of the body. The amount of urine is somewhat diminished; the solids are also diminished more or less, in proportion to the impaired appetite. Usually, a secondary affection of the kidney, as shown by albuminuria, is present as well. In the majority of cases, the urine is pale and feebly acid, but there are many exceptions.

In chronic diseases of the liver, the urine is high-colored, excessively acid, diminished in quantity, and of high specific gravity. The absolute amount of total solids, however, is diminished, and the diminution of urea is in direct proportion to the extent of the hepatic destruction. There is usually an abundant sediment of urates and calcic oxalate. The coloring matters are relatively, and the indoxyl absolutely increased. As a rule, phosphoric acid is diminished.

In chronic rheumatism, the urine is apt to resemble that of acute disease. It is high-colored, excessively acid, and contains an increase of urea. Otherwise, the solids are diminished. Calcic oxalate is generally present in the sediment.

In chronic gout, the uric acid is diminished during a paroxysm, but during the intermission it is increased.

In chronic diseases of the spine, the indoxyl and phosphates are increased.

In chronic diseases of the bones, the phosphates, especially the earthy phosphates, are increased.

In leukocythæmia the proportion of uric acid to urea is increased. The latter may or may not be diminished. In many cases there are concomitant fatty changes in the kidneys, as evinced by albuminuria, fatty epithelium, and fatty casts.

In chlorosis and anæmia, as a result of the diminished tissue metamorphosis, the urine is pale. The urea and uric acid are diminished, usually in proportion to the destruction of red globules.

In Addison's disease the urea is diminished and the indoxyl increased.

In scurvy and purpura hæmorrhagica, as a result of the destruction of the red-blood globules, hæmoglobinuria frequently occurs, and from an associated parenchymatous nephritis there is albuminuria, and in the sediment casts are found.

In phthisis, the urine follows the febrile type; it is high-colored, but the specific gravity is not especially raised. The solids are diminished, except the earthy phosphates, which are increased in proportion to the destruction of lung tissue. As a result of the impeded oxidative processes, uric acid is apt to be increased. There may also exist a secondary kidney affection, not unlike active hyperæmia.

In chronic organic disease of the heart, the urine is apt to be febrile in character. Both urea and uric acid are relatively increased. The urea is absolutely diminished, whereas the uric acid may be absolutely increased. In addition, a slight albuminuria exists, and in the sediment are found a few casts, — passive hyperæmia.

Following the general rule of effusions and exudations, the chlorides will be diminished in cases of *dropsy;* but when once absorption of the effusion takes place, they will increase to normal. With the increase of the dropsy, the urea increases and the urine becomes febrile in character; but as absorption occurs, there is an absolute increase of the normal solids.

In all dropsical cases there is usually some associated renal affection.

Extensive disease of the skin is usually accompanied by renal disturbances. In some cases the sulphates appear to be increased.

In cases of melanotic cancer, the urine is usually normal in color when passed, but on standing turns dark brown or black. This is probably due to the oxidation of some chromogenous substance as yet unknown. When the growth is increasing rapidly, this color change is not so frequently observed.

In cases of malignant disease affecting the ab-

dominal viscera, the urine is febrile in character. The urea and solids are, however, much diminished absolutely. Indoxyl is considerably increased as a rule. As in all cases of impaired oxidation, there is an abundance of urates and calcic oxalate in the sediment, and frequently some renal complication.

## CHAPTER VI.

### THE URINE AS AFFECTED BY LOCAL DISEASES.

WHEN the urinary tissues, upon whose anatomical integrity and physiological health the elimination of normal urine depends, become diseased, an examination of the urine furnishes the most valuable indications concerning the nature and location of that disease.

The changes which are due to pathological processes may be confined on the one hand to the kidney itself, or on the other to some portion of the urinary tract below the kidney. Finally, both the kidney and the urinary tract below it may be affected simultaneously, although the extent and severity of the pathological processes may be greater in the one than in the other.

#### DISTURBANCES CONFINED TO THE KIDNEYS.

The evidences of renal disturbance are in the first place albuminuria; in the second, modifications in the physical and chemical characters of the urine; and finally, the presence in the sediment of tissue-elements and casts which are suggestive of renal disintegration.

In a general way, it may be said that in each of the renal diseases these evidences are associated in a more or less typical way, and it is by the correct interpretation of this association that a diagnosis of each affection is made. Before passing on to a detailed description of these evidences as they occur in the different forms of kidney disease, it may be well to consider briefly some facts connected with the etiology and pathology of nephritis in general.

The intimate relation which has been shown to exist between the blood and the kidney finds expression, on the one hand, in the kidney alterations to which disease of the blood gives rise, and, on the other, in the changes of the blood and vascular apparatus which are produced by disease of the kidney. Since the kidneys not only separate the water from the blood, but also the solid products of retrograde metamorphosis, it is quite conceivable that any alteration of the latter, either in quantity or quality, will have a marked influence on the renal tissues. Then, again, it is clear that any essential disturbance, either functional or structural, of an organ so important in removing from the body the water and excrementitious matter, may bring about an alteration of the vascular constituents.

The first of these propositions (blood composition) is important, since it explains why it is that

renal complications are so frequently associated with or succeed general disturbances, the so-called nephritides due to "humors in the blood." Conspicuous among these are the nephritides of infectious disease. In scarlet-fever and diphtheria, for example, secondary renal troubles are so constant that they almost form a part of the picture of those diseases. In typhoid fever, recurrent fever, and fibrinous pneumonia, the kidney changes are not so constant, but do occur with such frequency that they may be regarded as possible complications. Not only in acute, but in chronic diseases, malaria and syphilis, secondary kidney changes occur.

With respect to the pathogenesis of these secondary complications, it is not always evident that the specific irritant is to be found in the kidney. In certain cases, e. g. embolic nephritis of ulcerative endocarditis, this would appear to be the case. In other cases, e. g. nephritis occurring at the end of acute fibrinous pneumonia, in which Nauwerck has proved the presence in the kidney of the capsule coccus, it may be probable. But in the most frequent form of infectious nephritis (scarlet-fever) no such evidence exists. Hence, in most cases it is probable that the nephritis is not so much due to the presence of the infectious agent in the kidney as to the action of some deleterious substance (ptomaine) developed in the course of the infection

which the kidney is eliminating from the blood. On the other hand, severe nutritive disturbances, which are developed in the course of chronic infectious diseases, may be the cause of secondary renal disease, e. g. the amyloid degeneration associated with pulmonary tuberculosis and syphilis.

Although the above cases are all secondary, yet there are many instances of nephritis which are undoubtedly primary. The nephritides due to exposure to wet and cold, or other indefinite cause, are examples of this class. Even here the cause may be an infectious one, which is localized in the kidney, or it may be a general toxæmia, the expression of which is local.

It is undoubtedly proved that many poisons which are coursing in the blood may be carried to the kidneys, and there give rise to extensive alterations. In some of these toxic nephritides the alterations in the kidney appear to be due to the direct, in others to the indirect, action of the poison in question. Thus, cantharides, turpentine, and chromic acid are directly harmful to the kidney tissue with which they come in contact, whereas it is probable that some other poisons do harm through the action of a decomposition product which is developed as a result of their presence in the body. The kidney changes associated with an intravascular destruction of red corpuscles (severe burns) is a case in point.

In certain chronic renal affections a similar cause (the presence of deleterious substances in the blood) seems not improbable. These substances may in some cases be derived from without, e. g. alcohol; and in others from within, e. g. the products of retrograde metamorphosis.

No sharp line between the various etiological factors can be drawn, and in many instances chronic renal disease fails of any satisfactory explanation.

Whether due to infectious, toxic, or unknown causes, the pathological alterations of the kidney are of two general types, according to the nature of the process, on the one hand, and to its situation in the renal tissue, on the other.

Among the former, disturbances of circulation, inflammation, and degeneration are to be included; and among the latter, changes which may be seated in the glomeruli, epithelium, or vascular and interstitial tissue.

Disturbances of circulation consist either in an increased amount of blood in the organ (hyperæmia), or in a diminution of the same (anæmia). Anæmia as an independent affection of the kidney is probably never more than temporary, and is unaccompanied by definite alterations in the urine. Further consideration of this condition is therefore unnecessary. Hyperæmia, on the other hand, has

been found to be a tolerably frequent condition, and accompanied usually by more or less definite signs. The increased amount of blood in the organ may be due either to an increased afflux, or to a diminished efflux. The former condition, because due to causes directly operative in dilating the vascular channels of the kidney, is called active hyperæmia, whereas the latter, because due to causes preventing the usual outflow of blood from the organ, is called passive hyperæmia or passive congestion.

Hyperæmia is one of the essential features of every acute inflammation; hence it happens that every inflammation of the kidney must have passed through the stage of active hyperæmia. Not only this, but the condition of hyperæmia persists so long as the inflammation is active, and differs only in degree. The same causes, then, which produce a nephritis, are when less severe causative of active hyperæmia. It follows that the point at which a severe hyperæmia becomes a mild but true inflammation (nephritis) is often quite indefinite, and a diagnosis based on an examination of the urine alone must in such cases be equally uncertain.

Besides the hyperæmia, which may be so severe as to cause rupture of the vessels (hemorrhage), inflammation of the kidneys is also accompanied by round-cell exudation and secondarily degenerative changes. The exudation affects chiefly the

interstitial tissue and vessel walls, whereas the degeneration is confined almost wholly to the epithelium.

Although inflammatory processes may bring about secondary degenerative change, it is equally true that degenerative change may in the end lead to inflammation. In either case, the inflammatory process is limited, as above suggested, to the vascular and interstitial tissue, and the degenerative process to the epithelium. In this connection, the fatty kidney due to phosphorus poisoning, severe general anæmia, and cholera, i. e. disturbances of nutrition, are to be distinguished from true inflammations.

Upon such grounds as have been suggested, a classification of kidney inflammations has been made; viz. parenchymatous, or those in which the epithelium is affected, and interstitial, in which the pathological processes are confined to the renal stroma and blood-vessels. Such a classification is, however, purely empirical; first, because in the parenchymatous class there is a degeneration and not an inflammation of the secreting cells, although an inflammation of the stroma may coexist; and secondly, because it is rare that an interstitial inflammation is not accompanied or followed by some parenchymatous change. Finally, although the classification includes parenchymatous degenera-

tions, it does not include a degeneration of the vascular and interstitial tissue, i. e. Amyloid.

Hence the anatomical classification is not wholly satisfactory; but inasmuch as it is the one generally adopted and best understood, it will suffice here.

In the following descriptions of the urine as it varies in the different renal diseases, so much of the etiology and pathology has been introduced as, it is hoped, will serve to make the character of the urine more readily understood.

ACTIVE HYPERÆMIA (catarrhal nephritis, parenchymatous degeneration, "cloudy swelling") is simply an acute congestion of the kidney due to some slight irritation, and when uncomplicated and without permanent cause is only a temporary affection, disappearing completely within a few days.

Among the causes of active hyperæmia are the presence in the urine of any irritant, either chemical or zymotic; the long continued elimination of concentrated urine, or urine containing bile pigment or concretions; any cause whereby the kidney is overworked, e. g. chronic lung diseases and impaired action of the skin; intestinal disturbances; and extension to the kidney of an irritation or inflammation present in the lower membranes, — pelvis or bladder.

*The Characters of the Urine.* — These vary somewhat with the cause; e. g. if the active hyperæmia

is due to some acute febrile disease, the peculiarities of febrile urine are observed, viz. high color, increased specific gravity, etc., with or without diminution of the chlorides; if due to chronic disease, the urine is pale in color, of diminished specific gravity, etc.; if due to concretions, particles will be found in the sediment. In the majority of instances, however, the urine is concentrated and of high specific gravity, but this is not essential to the diagnosis. More positive features are the presence of a slight trace of albumen, and in the sediment more or less free blood, an excess of renal cells frequently brownish in color, a few pure hyaline and fine granular casts, to which blood globules and renal cells may be adherent, and finally occasional blood and epithelial casts.

In severer cases the albumen may be increased in amount, i. e. $\frac{1}{8}$ to $\frac{1}{4}$ of 1%, as well as the number of casts, which may include those of the brown granular and fibrinous variety. Under such circumstances, it cannot be positively affirmed, by the examination of a single specimen, whether it is a case of active hyperæmia or acute nephritis. If it is a simple active hyperæmia, the excess of albumen and casts rapidly disappears, and within a few days the ordinary characters of active hyperæmia are established.

When the exciting cause is persistent and the hy-

peræmia becomes long continued, fatty changes of the epithelium are induced, and as a result fatty cells and fatty casts may be encountered in the sediment.

If due to a severe attack of fever, the hyperæmia disappears with convalescence, and the quantity of urine for a time exceeds the normal. Under such circumstances, it may be difficult by an examination of the urine to distinguish between a hyperæmia and a recovery from acute nephritis, since it differs from an acute nephritis, as has been said, only by the usually less extent and diminished intensity of the pathological process.

Most cases terminate in recovery.

PASSIVE HYPERÆMIA (chronic passive congestion, cyanotic induration) is characterized anatomically by a condition of venous stasis, affecting, according as the cause is local or general, one or both kidneys. The blood-vessels, especially on the venous side, are markedly distended with blood; the connective tissue, in which the vessels run, is increased in amount; and at times the epithelium of the tubules undergoes more or less degeneration. Less arterial blood than usual flows through the kidneys, and the excess of blood which is present is largely venous in a more or less quiescent state. Under such conditions, a decreased flow of urine, a diminution of its solids, and the presence of albumen, become easily intelligible.

*Causes.* — The commonest causes of passive hyperæmia are pulmonary affections and uncompensated valvular diseases of the heart, in which the blood is prevented from passing through these organs in normal amount. The result is a general backing up of the venous blood in the right cavities of the heart, the great veins emptying into the right heart, and thence all through the body. The kidneys therefore share the common fate.

Among local causes are thrombosis of the ascending vena cava above the point at which the renal veins enter it, or thrombosis of the renal veins themselves; and pressure, as by a tumor, — new growth, or in females a pregnant uterus, — upon these same venous trunks at some point in their course toward the heart.

In pregnancy, the pressure is not so extensive as to cause an absolute decrease of the total solids, although the urine may be pale, and contain as much as ½ of 1% of albumen, together with hyaline and fine granular casts of large diameter. It cannot be positively affirmed that organic disease of the kidney exists, although such cases generally terminate in puerperal convulsions, followed by a genuine acute nephritis.

*Characters of the Urine.* — In general, it is diminished in amount; of high specific gravity (it may, however, be low); contains a slight trace of

albumen; there is an absolute diminution of solids, and a relative increase of some (the urea and uric acid may be absolutely increased). The amount of chlorides will depend on the amount of effusion, as has elsewhere been explained. The sediment will contain hyaline and fine granular casts of small diameter, a virtual absence of blood and no excess of renal epithelium.

Owing to the nature of its causes and its chronic course, passive hyperæmia does not admit of a favorable prognosis, but by proper treatment, directed to the underlying causes, temporary improvement may be obtained.

ACUTE PARENCHYMATOUS NEPHRITIS (acute diffuse nephritis, acute Bright's disease) is a true inflammation of the kidney. It may be due to long continued irritation (persistent active hyperæmia), exposure to cold and wet, or it may be associated with many of the acute infectious diseases, notably scarlet-fever, diphtheria, measles, typhoid, typhus, recurrent, and yellow fevers, fibrinous pneumonia, septicæmia, and acute articular rheumatism.

Anatomically the changes vary a great deal as to the particular region affected, their extent or diffusion, and the nature and severity of the cause. In many cases, e. g. scarlet-fever, only the glomeruli appear to be affected. In these there is a swelling of the epithelium, granular infiltration of the

capillary wall, and exudation under the capsule of Bowman. Oftener, however, there is in acute nephritis more or less round-cell or hemorrhagic infiltration into the connective tissue and the space between the capsule of Bowman and the glomerulus. The epithelium of the uriniferous tubules undergoes granular degeneration (cloudy swelling) and subsequently becomes fatty degenerated. The lumen of the tubules is plugged with extravasated blood globules, desquamated epithelium, and solidified albuminous material (casts). Physiologically, alterations in the nutrition of the tissues of the glomeruli, whereby their porosity or permeability is increased, is causative of albuminuria, and, as a result of inflammatory processes, both the pressure and rapidity of the blood stream in the glomeruli are diminished.

It is quite clear that, in proportion to the extent and severity of the changes enumerated above, the urine will be albuminous, diminished in amount, colored (blood pigment), and laden with renal cells, blood corpuscles, and casts. As the disease progresses, these characters vary, and, in accordance with that variation, acute nephritis may be divided into three stages.

*First Stage.* — The amount of urine is considerably diminished, — 300–500 c.c. in 24°; dark brown or black in color, and usually acid in reaction. The

specific gravity varies. In a general way it follows the quantity of urine. If the tubules are plugged to any great extent, it follows that the urine cannot get out; hence the amount, as well as the solids, upon which the specific gravity depends, will be diminished together, and in about the same proportion. The specific gravity is also, to some extent, directly dependent on the amount of blood present. It may, therefore, be either high or low. The normal solids are absolutely diminished. The amount of albumen varies with the severity of the disease and the amount of obstruction in the tubules. It is usually $\frac{1}{4}$ to $1\frac{1}{2}\%$.

There is usually considerable brownish-colored sediment, the color being due to the free admixture of decomposed blood pigment. Upon examination, the sediment is found to contain a large quantity of free abnormal blood-globules, and numerous brown granular renal cells; also large numbers of blood, epithelial, brown granular, and fibrinous casts, together with an occasional pure hyaline and fine granular cast.[1] If the inflammation is severe, pus corpuscles may be present.

*Second Stage.* — As the disease progresses, fatty changes ensue, and in a few days fatty elements — fatty renal epithelium and fatty casts — make their

[1] Pure hyaline and fine granular casts are found in the sediment of all the organic renal diseases.

appearance in the sediment, in addition to those elements already present. If the disease is to terminate fatally, the end comes during this stage; if recovery be the issue (most usual), a change in the urine occurs, and this turning point is called "beginning convalescence."

With the cessation of the inflammatory process, the blockade in the tubules is gradually raised; the urine begins to flow more abundantly, and increases rapidly. Concomitantly, the absolute amount of solids begins to increase, the brown color gives way to a "smoky" hue, and the chlorides reappear. As the amount of urine increases, the albumen decreases. There is a gradual, followed by a rapid, increase of the fatty elements, lasting one or two days. The brown granular and fibrinous casts decrease in number, and finally disappear; the hyaline and fine granular still persist. During this "period of transition," a positive diagnosis from an examination of the urine cannot be made. As beginning convalescence merges into established convalescence, the urine changes again.

*Third Stage.* — A reactional activity of the kidneys sets in. The amount of urine transcends the normal daily figure, and may rise as high as 2500 or 3000 c.c. The smoky color fades away, and the urine becomes pale. The solids, although relatively diminished, are now about normal. The

albumen has become diminished to a trace. In the sediment may be found hyaline and fine granular casts, an occasional blood cast, a few blood corpuscles and renal epithelial cells. The brown granular and fibrinous casts have entirely disappeared, and the fatty elements have followed suit, although a few may be discoverable still. With complete return to health, the urine decreases to the normal amount, the amber color returns, the albumen and casts disappear, and, in a word, it becomes normal again.

In acute nephritis, the return to health is not always progressive and uninterrupted. When convalescence is apparently established, a careless and at times slight exposure will be followed by a renewal of the inflammatory processes. Such interruptions are termed "acute exacerbations." Abundant hemorrhage from the straight tubules occurs, in consequence of which the urine becomes blood-red (normal blood) in color. The amount of urine diminishes, and the albumen increases slightly. In this condition a resemblance to active hyperæmia obtains.

Dropsy, a common accompaniment of nephritis, is rarely observed in active hyperæmia.

Although unusual, several exacerbations may be directly causative of a chronic parenchymatous nephritis.

CHRONIC PARENCHYMATOUS NEPHRITIS is rarely to be referred to a preceding acute nephritis; oftener it is associated with chronic wasting diseases, which are accompanied by long continued suppuration. In general, the etiology coincides pretty closely with that of fatty degeneration. What the nature of the specific irritant may be is as yet undetermined. The progress of the disease is gradual, and accompanied by no very obvious symptoms to the patient until it has reached a considerable degree of development. Thus the chronic nature of this form of nephritis is definitely established. Clinically, the patient suffers from digestive disturbances, lumbar pains, headache, and frequent micturition. He says that he is passing more water than usual, although this is to be attributed rather to the frequency with which he voids urine than to an absolute increase in the amount passed. Extreme pallor of the patient, and dropsy, are also striking symptoms.

Anatomically, the kidneys undergo various changes. Fatty degeneration of the epithelium of the tubules and glomeruli is the characteristic and most constant alteration. At times there is, in addition, a true inflammatory condition, characterized by hemorrhages, round-cell exudation into the connective tissue, desquamation of the renal epithelium, and solidification of albuminoid ma-

terial in the tubules. As in acute nephritis, there is a blockade of the eliminating channels, and a similar diminution in the amount of urine. In a few cases, if the interstitial tissue has been seriously involved, subsequent contraction of the kidney occurs, inducing in the urine all the characters of chronic interstitial nephritis.

Following upon the changes above described, the characters of the urine will vary according to the activity of the disease, hence a distinction between the active and passive stages is to be observed.

*Character of the Urine. — Active Stage.* — While the dropsy, which is invariably present, is increasing, the urine is high in color but not dark, diminished in amount,— 500 to 800 c.c. in 24°,— and exceedingly acid. The solids, with the exception of the chlorides (dropsy) and phosphates, are relatively increased in amount, but there is an absolute diminution of all, except perhaps uric acid. In this disease the albumen reaches the maximum limit, varying between ½ of 1% and 4 or 5%.

The sediment is usually abundant, consisting chiefly of amorphous urates, due to the concentration of the urine. In addition, there is a large number of fatty renal cells and compound granule cells. Fatty casts, often of large diameter, are numerous, as well as the pure hyaline and fine granu-

lar varieties. They may contain fragments of renal epithelium, and if the inflammation is conspicuously hemorrhagic they may be pigmented and contain blood globules, although this is more frequently dependent upon a coexistent active hyperæmia.

If the disease is to terminate fatally in this stage, numerous large waxy casts make their appearance in the sediment.

By proper treatment, the active symptoms may be checked, and the disease rendered less active; in this case the character of the urine changes.

*Passive Stage.*—If the dropsy is not increasing, and the patient is "holding his own," the amount of urine increases,—1300 or 1400 c.c. in 24°. The solids likewise increase, but not to the normal standard. They are still absolutely as well as relatively diminished. The color becomes pale, and in fact the urine merely exhibits the usual characters of chronic disease. The albumen diminishes somewhat. It may be ½ of 1% more or less. There is still considerable sediment, and, with the exception of an excess of urates, is like that found in the active stage.

The disease is not necessarily immediately fatal. After several years duration, atrophy of the renal tissue may occur. This fact leads many writers to speak of a *third stage*, in which the urine becomes almost identical with that accompanying chronic

interstitial nephritis. The essential points of difference are, that (*a*) the amount of urine is not so much increased as in interstitial, and (*b*) if it is a urine of chronic parenchymatous nephritis, fatty elements are occasionally found in the sediment.

CHRONIC INTERSTITIAL NEPHRITIS is, like the preceding, an affection of the kidneys, which develops slowly and insidiously, and frequently exists undetected until, months after the disease has become well developed, the patient is suddenly seized with a convulsion, which directs the attention of the physician to the kidneys.

The cause of the disease is as yet imperfectly understood. It is frequently found to be associated with gout, syphilis, and chronic lead poisoning, which suggest "chemico-toxic" influences. In many cases there is no sufficient cause to which the disease can be ascribed, and it must be regarded as idiopathic. Clinically, the patient suffers more or less from dyspepsia and headache, and, as the disease becomes well established, there is a gradually increasing frequency of micturition, which at last compels the patient to rise once or twice during the night and pass his urine. There is also an associated hypertrophy of the left ventricle of the heart, which induces more or less palpitation. In uncomplicated cases there is, as a rule, no dropsy.

The anatomical changes consist of a gradual destruction of the kidney cortex, which is due to the contraction of the hyperplased connective tissue. The inflammatory infiltration involves at first isolated areas of the cortical connective tissue, blood-vessels, and neighboring glomeruli. Subsequently, by contraction of the newly formed tissue, the surface of the kidney becomes markedly roughened or granular, corresponding to the areas of contraction. As the process extends, and the different islets of inflammation fuse together, the cortex becomes, after contraction, much reduced, and wellnigh obliterated. The kidney, as a whole, is reduced in size, may be to one fourth its original volume, and the granular appearance of its surface, alluded to above, has given to it the name of the small or contracted granular kidney.

The epithelium of the tubules has, meanwhile, suffered degeneration and disintegration. Associated with the processes going on in the kidneys, there is a change in the blood-vessels. The failure on the part of the kidney to eliminate the urinary constituents, means, of course, their retention in the vessels. The irritation of the latter, to which such a retention gives rise, is manifested by a general arterial spasm, followed by arterio-fibrosclerosis and consequent diminution of the vascular lumina. To meet this condition of affairs a com-

pensatory hypertrophy of the heart ensues, which is a characteristic feature in all cases of well developed interstitial nephritis.

The character of the urine depends directly upon these processes. In the early stages of the disease, when only isolated spots of the kidney are involved, little or no alteration of the urine is to be observed. By degrees, however, larger patches of tissue become affected, and many of the glomeruli and tubules are rendered useless for excretory purposes. The character of the urine gradually changes; it becomes, not diminished, but — owing to the compensatory hypertrophy of the heart and the remaining glomeruli, which are functional — increased in amount. The power of the epithelium to excrete the solid constituents is impaired, and consequently the total solids suffer diminution. Albumen in small amount will be present, and, as the renal tissue contracts, a few cells may be rubbed off, and appear, together with a few casts, in the sediment.

*Character of the Urine.* — In the early stages it varies slowly from the normal. The amount increases slowly; at the same time the normal constituents show upon examination no marked change, perhaps only a slight diminution. A trace of albumen may be discoverable, and, after careful search, an occasional hyaline and fine granular cast.

In this stage, the clinical examination of a specimen would not differ, save in the amount of urine, from that observed in a case of passive hyperæmia.

As the disease becomes more advanced, the urine becomes pale and is considerably increased (2000–4000 c.c.) in amount. The specific gravity, at the same time, decreases, — 1010 more or less; 1005 when far advanced. The normal solids are both relatively and absolutely diminished, with the exception of indoxyl, which remains relatively normal. This means, of course, an absolute increase, and interstitial nephritis is the only organic renal disease in which there is an absolute increase of indoxyl. The albumen measures $\frac{1}{4}$ of 1%, more or less.

In the sediment, which is very slight, are hyaline and fine granular casts of small diameter (larger ones may be found in well advanced cases), and possibly an occasional renal cell. The sediment is so slight that it is necessary to let the urine stand several hours to insure settling of the casts; and, furthermore, some care in the preparation of a slide will oftentimes be rewarded with a positive result, which might otherwise have been negative.

When the kidneys have become so much atrophied as to leave only six or twelve months of life, the urine again changes. The cardiac hypertrophy

can no longer overcome the destructive obliteration of the glomeruli and tubules, and the amount of urine gradually falls to normal, and perhaps slightly below, —1200–1300 c.c. In other respects, its characters remain unchanged, save that waxy casts may be found in the sediment. As a rule, the appearance of waxy casts is indicative of death within six or nine months.

For a short time before death, the excretion of urine is markedly diminished, even to complete suppression.

The disease is almost invariably fatal, and frequently prematurely so, from the rupture of atheromatous cerebral vessels, which cannot withstand the increased cardiac activity.

AMYLOID DEGENERATION of the kidney is not an inflammation, but probably a nutritive disturbance, whereby a peculiar bacon-like substance possessed of definite chemical reactions (i. e. stains mahogany-brown with iodine) makes its appearance in the cortex of the kidneys, affecting primarily the muscular coat of the afferent blood-vessels; then, in succession, the glomeruli, vasa efferentia, and vessels of the pyramids. The vessel walls become thickened, and the lumen diminished.

The causes of the amyloid change are not definitely understood. It is observed, however, to be associated with chronic pulmonary consumption,

long continued wasting diseases, chronic suppurations (joint disease), and syphilis. The diagnosis is usually made from the clinical history, and the discovery of amyloid change in other organs, especially in the liver and spleen.

*Character of the Urine.* — Examined clinically, the urine is found to possess all the features which characterize interstitial nephritis, and is often quite indistinguishable from that of the latter disease. The essential difference, so far as the urine is concerned, is a higher specific gravity on the average, because it contains a more nearly normal quantity of solids. The albumen, too, is liable to be more abundant in amyloid degeneration. In the beginning, however, there may be none; but as the degeneration progresses, the albumen appears, and gradually increases, even reaching 3%. The sediment is the same as that found in chronic interstitial nephritis.

It follows, therefore, that a quantitative estimation of the total solids is the only means whereby the urine of amyloid degeneration can be distinguished from that of interstitial nephritis.

Although the disease is incurable, the patient may live many years.

The different varieties of organic renal disease have now been described in their uncomplicated

form. More frequently, however, kidney diseases are combined with each other; under these circumstances, the diagnosis often becomes difficult and unsatisfactory.

The more common combinations are:

1. Chronic parenchymatous with interstitial nephritis (chronic diffuse nephritis).

As it is unusual for chronic disease to exist independently of some interstitial change, it is quite unnecessary to diagnose by urinary examination chronic diffuse nephritis. The amount both of urine and of albumen will be governed by the disease which predominates. For example, a nearly normal amount of urine containing $\frac{1}{2}$ of 1% of albumen and fatty elements would suggest a predominance of the parenchymatous process. As a rule, the course of chronic parenchymatous is more rapid than that of chronic interstitial nephritis.

2. Chronic parenchymatous nephritis with amyloid degeneration, the etiological factors of both these affections being very much the same.

Chronic parenchymatous nephritis complicated with amyloid degeneration cannot, by an examination of the urine, be distinguished from chronic diffuse nephritis. The detection of amyloid degeneration in the palpable viscera would render a diagnosis of amyloid complication in the kidney more probable.

In any combination, there may be a little acute nephritis superadded.

3. Chronic parenchymatous with acute nephritis.

In this case, the water is diminished in amount, the albumen increased, and in the sediment are found blood and fatty elements, also hyaline, blood, fatty, granular, and brown granular casts. By the examination of a single specimen it cannot be positively affirmed whether it is the above combination or a case of acute nephritis in the second stage. If the former, the prognosis would be grave; if the latter, favorable. To establish the diagnosis, a history of symptoms covering a couple of weeks would be indicative of acute nephritis, whereas if chronic the symptoms would cover a considerably longer period. If, after repeated examinations, the fatty elements should presently disappear, it would be indicative of an acute nephritis, whereas the persistence of the fatty elements and a disappearance of the blood would prove the alternative. Finally, in this combination the amount of urine does not, as in convalescence from simple acute nephritis, exceed the normal.

SENILE ATROPHY of the kidneys is, as its name implies, an affection of old age. It is a kind of slow interstitial nephritis. The changes, however, are not limited, as in interstitial nephritis, to the cortex, but involve both cortex and pyramids

alike. The urine resembles that of passive hyperæmia, viz. diminished quantity, high colored, not markedly increased specific gravity, slight albuminuria, and hyaline and fine granular casts in the sediment.

MALIGNANT DISEASE of the kidneys gives rise, as a rule, to no change in the urine, unless the circumscribed irritation provokes a slight active hyperæmia. It is rare that any portion of the growth is detected in the urine. Infrequently, as a result of ulceration, pus and blood may be found. Otherwise, the diagnosis of malignant disease is quite impossible.

ABSCESS OF THE KIDNEY. — In this affection, pus may be discharged into the tubules or renal pelvis. The character of the urine will vary according to the nature and situation of the abscess. A diagnosis cannot be made by an examination of the urine alone.

### DISEASES OF THE URINARY MEMBRANES BELOW THE KIDNEY PROPER.

PYELITIS is an inflammation of the mucous membrane lining the renal pelvis. It is caused by the extension downward of inflammatory processes from the kidney (acute nephritis), or upward from the bladder, especially if the latter contains ammoniacal urine (cystitis). Irritating sediment or

concretions are also a frequent cause of pyelitis. The disease itself may be acute or chronic.

*Acute Pyelitis.* — The urine is febrile in character, acid in reaction, and, if concretions are present, excessively so. The sediment is usually abundant, and contains pus and blood, varying in amount, usually considerable, with the extent and severity of the affection. The per cent of albumen varies with the amount of pus and blood present, — more in proportion to the quantity of blood, however, than to pus. During the early stages, cordate cells from the superficial layers of the pelvic mucous membrane, and, later, small round cells from the deeper layers, are present in the sediment. The presence of pus is quite characteristic of acute pyelitis. The pus corpuscles, mixed with blood globules and pelvic cells, are arranged irregularly in clumps. At times they are aggregated into thick, short cylinders, suggesting casts from the papillary ducts.

Not infrequently the inflammation extends to the straight tubules of the kidney, the evidence of which is the presence in the sediment of hyaline, epithelial, and granular casts. (Compare Prostatitis, page 177.) It is not important, practically, to differentiate between pyelitis and acute nephritis.

When the pyelitis is caused by the irritating

action of concretions, particles may be looked for in the urine.

*Chronic Pyelitis.*—If the disease becomes chronic, the urine changes. It is pale (unless hemorrhage occurs), slightly acid, diminished in amount, and contains an abundant sediment, which settles slowly, not in flocculent masses, but as a thin film which adheres to the glass and is with difficulty picked up with the pipette. The sediment consists chiefly of pus in clumps, numerous small round cells from the deeper layers of the renal pelvis, and more or less blood; there is always a little. If concretions are the cause of the pyelitis, fragments are present in the sediment. On the other hand, there is usually no sedimentary evidence when the pelvic inflammation is due to local morbid growths and tuberculous processes.

A calculus sufficiently large to obstruct the orifice of the ureter may cause a retention of urine in the renal pelvis. As the secretion of urine continues, the pelvis gradually becomes distended, giving rise to the condition known as *hydronephrosis;* or similarly, if the distention be largely due to pus, *pyonephrosis.*

Ureteritis, or inflammation of one or both ureters, is a very rare disease. Inflammation which is extending either up or down the urinary membranes usually skips the ureters. The common

cause of ureteritis is the passage of concretions. In simple cases, the urine itself is unaffected, but the sediment may contain, besides bits of concretions, spindle-shaped cells from the tissues of the ureter, and, in addition, blood and pus.

When there is a partial obstruction of the ureters, as may arise from the pressure of tumors, impacted concretions, and stricture of the urethra, the character of the urine is different. In such cases it is partially suppressed, — more or less anuria, — hence greatly diminished in amount. It is slightly albuminous, somewhat acid, and of low specific gravity. The solids are relatively and absolutely diminished. In the sediment may be found pus, blood, and cells from the seat of inflammation, and, after careful search, an occasional hyaline cast. This condition is, however, of rare occurrence. (Compare Anuria, page 134.) If the seat of obstruction is in the urethra, there usually is, in addition to the above, an inflammation of the bladder, or cystitis.

Cystitis, as has already been intimated, frequently occurs from an extension of the inflammatory process from the neighboring urinary tract, i. e. pyelitis or gonorrhœal urethritis. In many instances the inflammation is apparently induced by the presence of foreign bodies in the bladder, — notably calculi. It is to be observed, however,

that in such cases the cystitis is not so much dependent on the mere irritating influence of the stone as upon the introduction of unclean catheters and sounds used to determine its presence. Other cases of cystitis arise from stricture of the urethra, and paralysis of the vesicle sphincter. In the former instance there is a retention of urine in the bladder and an associated desire to micturate frequently. In the latter, there is a constant dribbling of urine. Under such conditions, the urethra contains a stagnating column of urine, and to this column the air, containing bacteria of decomposition, has direct access. As a result, the urine in the bladder soon becomes ammoniacal, and acts as a direct irritant upon the mucous membrane of the bladder. Finally, cystitis may be caused by the action of irritants eliminated in the urine (e. g. cantharides, certain foods, drinks, and infectious agents), or it may arise idiopathically, although very rarely, as a result of exposure to cold.

According to its nature and activity cystitis may be acute or chronic.

*Acute Cystitis.* — The quantity of urine is diminished, concentrated, and more or less bloody. The solids are relatively increased, and the per cent of albumen varies, as in pyelitis, with the amount of pus and blood present. During the first few days of the disease the urine is acid, but

very soon the urea undergoes decomposition within the bladder, and the urine becomes alkaline. The ammonia, to which the alkalinity is due, gives to the urine its distinctly ammoniacal odor, which, if detected as it is voided, is quite pathognomonic of cystitis.

A long continued acute cystitis may become chronic if the exciting cause persists, e. g. retention of vesicle calculi.

*Chronic Cystitis.* — In untreated cases, the urine is pale, ammoniacal, of low specific gravity (usually), very turbid, and contains an abundant sediment; frequently, if the amount of pus present is considerable, it is "ropy." The amount of albumen will, as in the acute form, depend on the pus and blood present. The sediment is only with some difficulty picked up by the pipette, and contains chiefly amorphous masses of bacteria, ammonium urate, triple phosphate, and disintegrated pus-corpuscles. If the specimen examined is a fresh one, normal blood and bladder epithelial cells may be found in the sediment. To examine the sediment, the fluid urine should be decanted from the ropy mass and allowed to settle.

In treated cases of chronic cystitis, the urine is not necessarily of alkaline reaction; in fact, it is usually acid and not ropy. In the sediment pus, blood, and bladder epithelium may be found.

In other respects, the urine is the same as in untreated cases.

An inflammation limited to the neck of the bladder is a not infrequent complication of gonorrhœa. In such cases, the urine is not alkaline, but acid. The sediment consists of blood and pus, together with an excess of cells from the neck of the bladder. There is no excess of bladder epithelium. Albumen in proportion to the amount of blood, usually only a trace, may be present.

PROSTATITIS, or inflammation of the prostatic portion of the urethra, may arise, like the preceding, from the upward extension of a gonorrhœa. It is also frequently caused by the passage of calculi, and in connection with a stricture of the urethra. An abscess of the prostate gland may discharge into the urethra, with evidences of a prostatitis.

The *character of the urine* is identical with that found in connection with pyelitis, and a differential diagnosis is only possible by a careful consideration of the cellular elements found in the sediment. In prostatitis there is an excess of cells from the prostatic urethra, together with an occasional cell from the neck of the bladder, and spermatozoa. The presence of casts from the straight tubules of the kidney is, on the other hand, indicative of pyelitis, and upon their presence the differential diagnosis is chiefly based. Rarely, casts of pros-

tatic ducts are found. These are, however, irregular in outline, much larger than renal casts, and in addition may have spermatozoa attached to them.

URETHRITIS is, as the name implies, an inflammation of the urethra. It is rarely necessary to examine the urine to establish a diagnosis of this disease. Most commonly urethritis is due to a local infection of the urethral mucous membrane by the gonococcus, but it may also proceed from irritation caused by the long continued elimination of irritants, e. g. cantharides and turpentine. Finally, it may occur in connection with infectious diseases. The urine, when voided, is at first cloudy, but as the products of inflammation are washed out of the urethra it becomes clear. In severe cases the urine may be bloody, as well as cloudy, and in the sediment are pus (in abundance when due to gonorrhœa), blood, and shreds of urethral epithelium.

BLOOD IN THE URINE. — When the urine contains much blood, a diagnosis from an examination of the urine is frequently a matter of great difficulty. Severe hemorrhages usually occur from the pelvis of the kidney and the neck of the bladder, in connection with the passage of calculi or the presence of morbid growths. If due to calculi, the *corpora delicti* are found in the sediment; but, as has been previously stated, morbid growths are seldom passed

with the urine save when so situated that bits of the neoplasm may be dislodged by the passage of a catheter, or caught in the eye of the instrument.

PUS IN THE URINE — When present in excess, pus is indicative of inflammation. It is not, *per se*, diagnostic of any one affection. To determine its source, it is necessary to consider the nature of the cellular elements with which it is associated. Even then, owing to the similarity of the various types of epithelium, it is not always easy to locate the inflammatory process. Especially is this the case among females, in whom a suppurative process in the urinary organs is always accompanied by an excess of vaginal epithelium, in addition to other cellular elements, e. g. epithelium from the bladder and renal pelvis. The especial features of distinction between bladder and vaginal epithelium have already been discussed (*vide* page 103). In addition, it may be stated that generally the amount of epithelium present is greater than can be accounted for by the amount of pus. With a cystitis, there is always pus in the urine. When unaccompanied by pus, an excess of epithelium is probably vaginal.

In pyelitis the characteristic clump formations consist of pus corpuscles mixed with small round cells only. Under such conditions, the excess of large polygonal plate cells may be ignored.

Thus, when the sediment contains an excess of blood or pus, together with a few other elements, the diagnosis, satisfactorily or unsatisfactorily, must be made by a process of inquiry similar to the above.

# APPENDIX A.

## METHOD OF RECORDING EXAMINATIONS.

For ordinary use, sheets of paper are printed in the manner indicated below, and as each test is made the result is indicated by abbreviations, more or less rational, more or less arbitrary, which are affixed to the spaces left for the purpose.

ANALYSIS OF URINE.

Name — Date

Amount in 24 hours = — Solids by sp. gr. =
Color = — Sp. gr. =
Odor = — Sed. =
Reaction =

Uph. = $\dot{U}$ = Cl = — E. P. =
Ixl. = $\bar{U}$ = Sf = — A. P. =

Alb. = — Sugar = — Bile pigment =
Quantitative. $\dot{U}$ = — $H_3PO_4$ =
Cl = — Sugar =

Sediment.

Diagnosis.

Remarks.

The abbreviations used upon the blank forms are: Uph. (urophæine), Ixl. or Ind. (indoxyl), Cl (chlorides), $\dot{U}$ (urea), $\bar{U}$ (uric acid), Sf. (sulphates), E. P. (earthy phosphates), A. P. (alkaline phosphates), sp. gr. (specific gravity), Sed. (sediment), Alb. (albumen), etc.

The same plan may be incorporated into book form at a proportionate cost, and for those who make numerous examinations and keep permanent records the book form prefaced by a lettered index is perhaps more serviceable and convenient than the separate sheets.

The common abbreviations used in recording results are: + for increased; — for diminished; N. for normal. For great increase or great decrease: gt. + and gt. —, respectively, may be used; similarly sl. + and sl. — for slight increase and slight decrease. Other abbreviations, according to the habit and convenience of the recorder, may equally well be adopted.

## Differential Diagnosis.

The diagnosis between the different diseases of the urinary apparatus is made chiefly by exclusion.

It has already been shown that, even in a single affection, the characters of the urine vary with the severity and extent of the process; furthermore, that urinary diseases exhibit a great tendency to combine with one another. Obviously, *an absolute standard*, to which an unknown specimen of urine should conform, is out of the question. In other words, a urinary disease is not accompanied by a urine of specific characters, but of characters which will vary; exhibiting now only evidences of a more or less intense form of a sin-

gle disease, now evidences of a more diffuse process, in which the characters of the dominant affection are the more obvious.

In order, then, to make a diagnosis, it is highly important in every case, first, to know the "typical" or possible characters which are commonly associated with each form of disease; and secondly, having made an accurate examination of an unknown specimen of urine, to harmonize so far as is possible the discovered characters with those known to be associated with this or that disease. Finally, it becomes possible only by the application of the above principles to say of an unknown specimen, "It probably belongs to this disease *because*, on the whole, it cannot belong to that."

To illustrate this method of making diagnoses, the following examples are offered, followed by a brief consideration of the diagnosis in each case.

1. Amount in 24 hours = 1000 c.c. Sp. gr. 1024.
   Color = high. Sed. much.
   Reaction = acid.
   Uph. = + $\dot{U}$ = + Cl = sl. − E. P. sl. +
   Ixl. = N. $\bar{U}$ = gt. + Sf = N. A. P. sl. +
   Alb. = 0. Sugar = 0. Bile pigment = 0.
   Sed. Amorphous urates.

2. Amount in 24 hours = 800 c.c. Sp. gr. = 1010.
   Color = smoky. Sed. = considerable.
   Reaction = acid.
   Uph. = − $\dot{U}$ = − Cl = N. E. P. = −
   Ixl. = + $\bar{U}$ = N. Sf = N. A. P. = −
   Alb. = 1%.
   Sed. Few free blood globules. Renal epithelium. Epithelial, blood, fibrinous, granular, and brown granular casts.

3. Amount in 24 hours = 1020 c.c. Sp. gr. = 1030.
Color = high.
Reaction = acid.
Uph. = N. $\dot{U}$ = N. + Cl = gt. + E. P. = N.
Ixl. = N. $\bar{U}$ = N. + Sf = gt. + A. P. = sl. −
Alb. = sl. trace.
Sed. Many uric acid crystals. Considerable blood and renal epithelium. Numerous hyaline casts, many of which have renal cells and blood adherent.

4. Amount in 24 hours = 470 c.c. Sp. gr. = 1030.
Color = high. Sed. = considerable
Reaction = acid.
Uph. = + $\dot{U}$ = gt. + Cl = − E. P. = N.
Ixl. = gt. + $\bar{U}$ = gt. + Sf = N. A. P. = −
Alb. = 2%.
Quant. $\dot{U}$ = 17.6. $H_3PO_4$ = 0.564.
Cl = 0.598. Sugar = 0.
Sed. Numerous hyaline, granular, and fatty casts. Fatty renal epithelium.

5. Amount in 24 hours = 1500 c.c. Sp. gr. = 1008.
Color = pale. Sed. = considerable.
Reaction = acid.
Uph. = − $\dot{U}$ = − Cl = − E. P. = −
Ixl. = − $\bar{U}$ = − Sf = − A. P. = −
Alb. = large trace.
Quant. $\dot{U}$ = 18.
Cl = 2.72.
Sed. Hyaline and granular casts.

6. Amount in 24 hours = 1230 c.c. Sp. gr. = 1012.
Color = sl. pale. Sed. = slight.
Reaction = acid.
Uph. = − $\dot{U}$ = − Cl = N. E. P. = −
Ixl. = N. $\bar{U}$ = sl. + Sf = N. A. P. = −
Alb. = very sl. trace.
Quant. $\dot{U}$ = 15.74. $H_3PO_4$ = 0.96.
Cl = 4.18.
Sed. An occasional pure hyaline cast.

7. Amount in 24 hours = 8450 c.c. Sp. gr. = 1012.
Color = pale. Sed. = slight.
Reaction = acid.
Uph = much − $\dot{U}$ = − Cl = − E. P. = −
Ixl. = N. $\bar{U}$ = − Sf = N. A. P. = sl. −
Alb. = ½%.
Quant. { $\dot{U}$ = 35.9. $H_3PO_4$ = 2.24.
Cl = 10.4.
Sed. Hyaline, granular, and waxy casts.

8. Amount in 24 hours = 2400 c.c. Sp. gr. = 1010.
Color = pale. Sed. = considerable.
Reaction = acid.
Uph. = − $\dot{U}$ = − Cl = − E. P. = −
Ixl. = N. $\bar{U}$ = N. Sf = sl. + A. P. = +
Alb. = $\frac{1}{10}$%.
Sed. Normal blood and pus, excess of vaginal epithelium. Hyaline and granular casts.

9. Amount in 24 hours = 500 c.c. Sp. gr. = 1024.
Color = high. Sed. = considerable.
Reaction = acid.
Uph. = N. $\dot{U}$ = + Cl = N. E. P. = N.
Ixl. = sl. + $\bar{U}$ = + Sf = N. A. P. = N.
Alb. = very sl. trace.
Quant. { $\dot{U}$ = 17.5.
Cl = 4.08.
Sed. Hyaline casts. Excess of mucus.

10. Amount in 24 hours = 1200 c.c. Sp. gr. = 1019.
Color = N. Sed. = considerable.
Reaction = acid.
Uph. = N. $\dot{U}$ = N. Cl = N. E. P. = N.
Ixl. = N. $\bar{U}$ = N. Sf = N. A. P. = −
Alb. = large trace.
Quant. { $\dot{U}$ = 25. $H_3PO_4$ = 2.15.
Cl = 4.60.

Sed. Renal epithelium, some of which is fatty. Hyaline and granular casts, some having oil globules adherent An occasional epithelial and fatty cast. Occasional blood globule, both free and adherent to some casts.

11. Amount in 24 hours = 1150 c.c — Sp. gr. = 1012.
Color = smoky. — Sed. = considerable.
Reaction = acid.
Uph. = N. — $\dot{\bar{U}} = -$ — Cl = — — E. P. = N.
Ixl. = + — $\bar{U} = +$ — Sf = N. — A. P. = N.
Alb. = 1½ to 2%.
Sed. Epithelial, fibrinous, hyaline, fine granular, and fatty casts. Renal cells, some of which are fatty. Numerous blood globules, some pus.

12. Amount in 24 hours = 1350 c.c. — Sp. gr. = 1015.
Color = pale.
Reaction = acid.
Uph. = — — $\dot{\bar{U}} = -$ — Cl = N. — E. P. = —
Ixl. = sl. — — $\bar{U} = +$ — Sf = N. — A. P. = N.
Alb. = 1%.
Quant. $\begin{cases} \dot{\bar{U}} = 22.6. \\ Cl = 6. \end{cases}$ $H_3PO_4 = 1.2.$
Sed. Numerous hyaline, coarse, and fine granular casts. Fatty and epithelial casts. Considerable fatty renal epithelium. Little pus, blood, and bladder epithelium.

13. Amount in 24 hours = 1850 c.c. — Sp. gr. = 1012.
Color = pale. — Sed. = considerable.
Reaction = acid.
Uph. = — — $\dot{\bar{U}} = -$ — Cl = sl. — — E. P. = —
Ixl. = +. — $\bar{U} = N.$ — Sf = N. — A. P. = —
Alb. = ⅛%.
Quant. $\begin{cases} \dot{\bar{U}} = 23.4. \\ Cl = 4.34. \end{cases}$ $H_3PO_4 = 1.51.$
Sed. Numerous hyaline, fatty, and granular casts. Fatty renal epithelium. Compound granule cells. Pus corpuscles free and in clumps. Normal blood globules and small round cells.

14. Amount in 24 hours = 600 c.c. Sp. gr. = 1012.
Color = sl. smoky. Sed. = considerable.
Reaction = acid.
Uph. = — $\dot{U}$ = — Cl = — E. P. = —
Ixl. = N. $\bar{U}$ = Sf = A. P. = —
Alb. = ½ to 1%.
Sed. Numerous large granular, coarse granular, fatty, and waxy casts. Granular and fatty renal epithelium. Compound granule cells. Cholesterine crystals. Blood.

15. Amount in 24 hours = 1770 c.c. Sp. gr. = 1014.
Color = sl. pale. Sed. = considerable.
Reaction = acid.
Uph. = N. $\dot{U}$ = — Cl = sl. — E. P. = —
Ixl = sl. — $\bar{U}$ = N Sf = N. A. P. = —
Alb. = $\frac{8}{10}$%.
Sed. Much blood; little free renal epithelium; hyaline and granular casts; few blood and epithelial casts; very few fatty casts.

16. Amount in 24 hours = 1760 c.c. Sp. gr. 1015.
Color = pale. Sed. = considerable.
Reaction = acid.
Uph. = — $\dot{U}$ = — Cl = N E. P. = N.
Ixl. = + $\bar{U}$ = + Sf = N. A. P. = N.
Alb. = ¼ to ½%.
Sed. Hyaline, coarse, fine granular, and fatty casts. Renal epithelium, much of which is fatty.

17. Amount in 24 hours = 1800 to 2400 c.c. Sp. gr. = 1015½.
Color = sl. pale. Sed. = considerable.
Reaction = acid.
Alb. = 1%.
Sed. Numerous hyaline casts, all with more or less fat drops adherent. No fatty casts; an occasional granular cast. Renal epithelium, most of which is fatty. Small quantity of pus, and numerous compound granule cells.

18. Amount in 24 hours = 1360 c.c. Sp. gr. = 1022.
Color = high. Sed. = considerable.
Reaction = acid.
Uph. = N. $\dot{U}$ = + Cl = N. E. P. = N.
Ixl. = N. $\bar{U}$ = + Sf = N. A. P. = N.
Alb. = sl. trace.
Quant. { $\dot{U}$ = 35.02. $H_3PO_4$ = 8.250.
Cl = 19.30.
Sed. Chiefly uric acid crystals. Numerous hyaline and granular casts, many of which are of large diameter and have blood globules and renal cells adherent. Little free blood and renal epithelium.

19. Amount in 24 hours = 2350 c.c. Sp. gr. = 1012.
Color = pale. Sed. = slight.
Reaction = acid.
Uph. = − $\dot{U}$ = − Cl = − E. P. = −
Ixl. = − $\bar{U}$ = − Sf = − A. P. = −
Alb. = ¼%.
Quant. { $\dot{U}$ = 28.8.
Cl = 3.24.
Sed. Chiefly hyaline and fine granular casts. An occasional blood, epithelial, and fatty cast. Little free blood. Fatty and granular renal epithelium.

20. Amount in 24 hours = 1920 c.c. Sp. gr. = 1013½.
Color = N. Sed. = considerable.
Reaction = acid.
Uph. = N $\dot{U}$ = N. Cl = − E. P. = −
Ixl. = N. $\bar{U}$ = sl. + Sf = N. A. P. = N.
Alb. = sl. trace.
Quant. { $\dot{U}$ = 41.5. $H_3PO_4$ = 4.20.
Cl = 7.52.
Sed. Large amount of uric acid. Numerous hyaline and fine granular casts. An occasional epithelial and fibrinous cast. Little free blood and renal epithelium.

21. Amount in 24 hours = 1150 c.c. Sp. gr. = 1013.
Color = N. or sl. pale. Sed. = considerable.
Reaction = acid.
Uph. = – $\bar{U}$ = N. Cl = sl. – E. P. = –
Ixl. = – $\bar{U}$ = Sf = A. P. = N.
Alb. = sl. trace.
Sed. Much pus, free and in clumps. Bladder epithelium, free and in shreds. Very little free abnormal blood. Little renal epithelium, some of which is slightly fatty. Occasional medium and large round cell. Occasional caudate cell. Fine granular, brown granular, blood, and fibrinous casts. Occasional pure hyaline casts (of small and medium diameter), some with blood, pus, and fat drops adherent.

22. Amount in 24 hours = 1275 c.c. Sp. gr = 1020.
Color = N. Sed. = considerable.
Reaction = acid.
Uph. = N. $\bar{U}$ = N. Cl = N. E. P. = N.
Ixl. = N. $\bar{U}$ = + Sf = N. A. P. = –
Alb. = large trace.
Quant. { $\bar{U}$ = 27.488. $H_3PO_4$ = 1 976.
Cl = 8.504.
Sed. Few abnormal blood globules. Excess of renal cells, some of which are fatty. Considerable number of hyaline and granular casts, some of which have a few blood and oil globules and renal cells adherent.

## The Inferences.

1. A simple concentrated urine of febrile character. The increase of uric acid suggests insufficient oxidation, and in combination with the diminution of the chlorides might fairly illustrate a urine of pneumonia.

2. The character of the sediment limits the process to the kidney and the amount of urine to the parenchym-

atous affections. The characteristic fatty elements of the chronic parenchymatous nephritis are absent, whereas everything about the urine is typical of acute nephritis in its early stage.

3. A case of active hyperæmia due to the irritating action of uric acid crystals.

4. The amount of urine and the character of the sediment limit the diagnosis to a parenchymatous affection, either the chronic form or the acute in the fatty stage. Were it the latter, one would expect less albumen and more urine; hence the probability is that it is a case of chronic parenchymatous in the active stage.

5. The great diminution of the solids, the small amount of albumen, and the character of the sediment suggest unquestionably chronic interstitial nephritis.

6. Here again the case seems to be one of chronic interstitial nephritis, although in both this and the previous case the possibility of advanced amyloid degeneration cannot be definitely excluded.

7. The quantity of the urine alone limits the possibility to four conditions, viz. recovery from acute nephritis, interstitial, amyloid degeneration, and diffuse nephritis. Waxy casts are not as a rule associated with acute disease, and acute nephritis is very improbable. Were it not for the known quantitative amount of solids, amyloid degeneration and interstitial nephritis could not be differentiated; but the almost normal quantity of solids excludes interstitial, and therefore diffuse nephritis, and suggests unquestionably amyloid degeneration, for in this disease the eliminating function is not for a long time materially embarrassed.

8. In this case the diagnosis lies between interstitial nephritis and amyloid degeneration; without a quantitative estimation of the solids, a positive diagnosis cannot be made. The absolute increase of indoxyl is more suggestive of interstitial, than the greater per cent of albumen is of amyloid degeneration. The excess of vaginal epithelium may have a causal relation to the blood and pus, and in all probability is due to a concomitant menstrual flow, or some irritation about the cervix uteri.

9. In this case the sediment is not indicative of an irritation nor inflammation, hence neither a nephritis nor yet an active hyperæmia. The only possibility is therefore a passive hyperæmia, the characters of which it best fulfils.

10. The general characters of the urine suggest active hyperæmia, acute nephritis in the fatty stage, and chronic parenchymatous nephritis. As against the last affection there is the presence of renal cells and blood, the lack of positive and characteristic fatty elements, the relatively small amount of albumen, and a rather large quantity of urine. It is quite safe to exclude the chronic parenchymatous disease. If it were a case of active hyperæmia, one would expect naturally a higher specific gravity, and, unless a very severe case, the absence of fatty elements; and finally, the presence of some bit of concretion or crystalline form to which the irritation might be ascribed. In the second stage of acute nephritis the urine is characterized by an increase in amount, together with an increase of the specific gravity, diminution of albumen, and the appearance of fatty elements in the sediment. These characters

are present in this case, and although in severe cases brown granular and fibrinous casts may be present, their absence does not preclude the diagnosis of acute nephritis passing through the fatty stage.

11. A more typical example of the former.

12. Another case of acute nephritis in the second stage.

13. The amount of urine excludes everything but recovery from acute or interstitial nephritis, amyloid degeneration, and diffuse nephritis. The abundance of fatty elements in the sediment and the compound granule cells are very suggestive of chronic parenchymatous, yet the quantity of urine and the per cent of albumen are not in conformity with this view. The increased amount of urine, the diminution of the solids, and the relatively small quantity of albumen favor interstitial. Hence, if both these coexist, the conditions will be satisfied, and the diagnosis of diffuse nephritis will be the result. The pus and small round cells are equally indicative of a complication with pyelitis or prostatitis, but the disease of the kidney makes it more probable that it is the pelvis that has become involved.

14. The excess of fatty elements in the sediment makes a diagnosis of chronic parenchymatous almost certain; yet the smoky color of the urine and the presence of blood in the sediment bespeak an acute process or exacerbation, which in all probability has occurred. The elimination of cholesterine crystals may have caused irritation of the renal tissue.

15. As in cases 7 and 13, the diagnosis lies between interstitial nephritis, amyloid degeneration, diffuse, and

recovery from acute nephritis. Without a quantitative estimation of the solids, no positive diagnosis between these possibilities can be made. If it were a case of recovery from acute nephritis, it would be natural to expect a higher specific gravity, and not a considerable amount of blood. On the other hand, it is not usual for fatty casts to exist in the sediment of interstitial nephritis or amyloid degeneration. If it were a diffuse nephritis, a greater quantity of fatty elements would in all probability be present. Some combination, therefore, may be assumed to exist. The quantity of urine, the low specific gravity, and the per cent of albumen, are equally in favor of interstitial nephritis and amyloid degeneration, whereas the blood, renal epithelium, and fatty casts are suggestive of an acute nephritis in a stage of beginning convalescence; and on the whole the conditions are best satisfied by assuming that an acute nephritis is superimposed upon an interstitial nephritis or amyloid degeneration.

16. The same considerations hold in this case as in the last, but here the fatty elements predominate, whereas the traces of acute disease are wanting. Aside from the quantity of urine, its characters are not incompatible with chronic parenchymatous nephritis; but the quantity cannot be excluded from the consideration, and in all probability a combination of interstitial (or amyloid degeneration) and chronic parenchymatous nephritis exists. It may be considered, therefore, to be a case of diffuse nephritis.

17. As in the two preceding cases, the same exclusions may be made. Like the last, fatty elements predominate, which make the consideration of chronic

parenchymatous nephritis imperative. There is, too, a relatively high per cent of albumen, which, without the signs of a recent active inflammation, make an acute nephritis improbable. The quantity of albumen is rather high for interstitial nephritis, although not for amyloid degeneration or chronic parenchymatous nephritis. The combination of the latter disease with interstitial nephritis or amyloid degeneration may be said to exist, but without a quantitative estimation of the solids, it cannot be positively affirmed with which the parenchymatous process is combined.

18. The uric acid crystals furnish the key of the situation. Aside from the albumen and sediment, the urine, as the quantitative estimation of the solids shows, is not abnormal. The sediment, however, is indicative of a slight irritation, which may be readily accounted for by the action of the uric acid crystals. Therefore an active hyperæmia due to the irritation caused by these crystals is quite sufficient as a diagnosis.

19. Here, again, the same exclusions as in cases 7, 13, 15, 16, and 17 may be made. It is unnecessary to go over again the same considerations as were made in those cases. The diminution of the normal constituents is in a great measure relative, although some absolute diminution also exists. The blood and epithelial casts indicate the existence of an acute process, and the fatty elements that the acute process has in a measure subsided, i. e. that it has progressed to the second or fatty stage. In fact, the features of acute nephritis in its fatty stage are typically illustrated. It cannot be positively affirmed, however, whether an interstitial or amyloid process coexists.

20. The absolute amount of solids excludes interstitial nephritis, amyloid degeneration, and, together with the absence of fatty elements, diffuse nephritis. Recovery from acute nephritis seems to be pretty well established. The excess of uric acid may be due to some defect of the oxidative processes or other cause of increased elimination of uric acid, but in all probability has no immediate relation to the pathological processes.

21. The character of the sediment alone is indicative of some active inflammatory process not confined to the kidney. The pus, caudate, and small round cells signify a destructive process connected with the renal pelvis and the casts, — that the renal tissue itself has been involved. The bladder epithelium and large round cells show, too, that the bladder and its neck have not escaped in the diffuse process. It cannot be affirmed which of the affections is primary. The indications at present are that a pyelo-nephritis exists which may have originated in cystitis. The per cent of albumen is not sufficiently large to indicate any considerable involvement of the renal tissue, and furthermore it is not greater than might readily be accounted for by the pus and blood.

22. The process is evidently acute, but it has lasted long enough for fatty changes to occur. Fatty elements alone are associated with severe cases of active hyperæmia, and acute and chronic parenchymatous nephritis. They are not, however, sufficiently numerous, nor is there so high a per cent of albumen, as to suggest the chronic nephritis. Between a severe form of active hyperæmia and an acute nephritis no positive

diagnosis in many instances can be made. Such seems to be the case here. On the one hand, during the fatty stage of acute nephritis one might expect a larger quantity of urine, as well as a larger per cent of albumen, than are present in this case. On the other hand, it is rare, although not impossible, for fatty changes to occur in active hyperæmia without evidences of a more intense irritative process. While it is impossible to say to which this case is to be referred, yet on the whole the present indications are more in favor of active hyperæmia than of acute nephritis.

# APPENDIX B.

## TABULAR ARRANGEMENT OF THE CHARACTERS OF THE URINE IN THE MORE IMPORTANT URINARY DISEASES.

For the purposes of easy reference, those features of the urine upon which the diagnosis is based have been arranged in tabular form, and incorporated into the following pages. While, as has so often been remarked, it is impossible to make any hard and fast distinctions as to what may properly constitute this or that disease, yet it is often convenient to see at a glance a group of tolerably constant symptoms, to which those obtained from a clinical examination may be quickly compared. In all cases, after a thorough comprehension of the nature of the different forms of disease, a thoroughly consistent deduction concerning the features discovered in an unknown specimen is far superior to any mechanical adaptation of symptoms to a table.

| Disease. | Quantity. | Color. | Sp. Gr. | Solids. | Alb. | Sediment. |
|---|---|---|---|---|---|---|
| Active Hyperæmia | — N. or +, usually — | *high* or pale | *high* or low | + or — (chlorides may or may not be diminished) | sl. trace in severe cases, ⅛–¼% | Free blood and renal cells, frequently colored more or less brown. Casts. Hyaline and fine granular, with blood globules and renal cells adherent. Occasional blood and epithelial casts. Brown granular and fibrinous casts in addition to the above. |
| Passive Hyperæmia | — (600–1000 c.c.) | high or pale | usually high (1030) | about normal absolute — relative + (U and Ū may be absolutely +) chlorides follow the effusions | sl. trace | Virtual absence of blood, no excess of renal cells. Casts. Hyaline and fine granular (of small diameter). Rarely a blood and epithelial cast. |
| Acute Par. Nephritis 1st stage . . . | — (300–500 c.c.) | dark brown (smoky) or black | *high* or low, according to occlusion of tubules, amount of blood and albumen. | absolutely — relatively + | ¼–1½% | Brown-colored. Free abnormal blood and an excess of renal cells colored ± brown. Casts. Blood, epithelial, brown granular, and fibrinous. Occasional hyaline and fine granular. |
| 2d stage . . . | increase (800–1000 c.c.) | light smoky | less than N. | increase (chlorides reappear) | ¼–½% | Fatty elements, cells, and casts. The hyaline and fine granular casts persist while brown granular and fibrinous disappear. |
| 3d stage . . . | + (2500–3000 c.c.) | N. or pale | low | relatively — absolutely about N. | trace | Hyaline and fine granular casts, an occasional blood cast, a few blood globules and renal cells. A few remaining fatty elements. |
| Chronic Par. Nephritis Active stage . . | — (500–800 c.c.) | high | high (1026–8) | relatively + (except Cl and P) absolutely — (except Ū) | ½–5% | Considerable amorphous urates. Fatty renal epithelium and compound granule cells. Casts. Fatty (of large diameter often), hyaline and fine granular. Near the fatal termination, waxy casts. |

| | | | | | | |
|---|---|---|---|---|---|---|
| Chronic Par. Nephritis, Passive stage . . | increase (1300–1400 c.c.) | pale | low | rel. and abs. — | ¼–½% ± | Same as in active stage. No excess of urates. |
| Chronic Interstitial Nephritis | In the early stages the urine varies but slowly from the normal. | | | | | |
| 2d stage . . . | + (2000–4000 c.c.) | pale | low (1010 ±) | rel. and abs. — except indoxyl which is rel. N. ∴ abs. + | ½% ± | An occasional renal cell. Casts. Hyaline and fine granular (small, medium, and in advanced cases, large diameter). |
| 3d stage . . . | decrease N. or — | pale | low (1005 ±) | ditto | ½% ± | Same with waxy casts previous to the fatal termination. |
| Amyloid Degeneration | + (2500–4000 c.c.) decreases before death | pale | low, but on the average higher than in interstitial | more nearly normal ± U diminished. | sl. trace progresses to 8% ¼–½% usually | Same as Interstitial. |
| Pyelitis, Acute . . (general febrile characters) | — | high | + | N. or — | trace varies with the pus and blood | Considerable pus and blood. Caudate cells from superficial layers of pelvis during early stages. Bits of concretions (if due to these). Characteristic arrangement of pus, blood, and cells together in clumps. If tubules of kidney are involved, hyaline, epithelial, and granular casts. |
| Pyelitis, Chronic . . | — | pale | — | . . . . . | ditto | Similar to the acute stage. Not so abundant, and in place of caudate cells are small round cells from deeper layers. |
| Cystitis, Acute . . | — at first *acid* then *alkaline* | high | + | rel. + | same as in Pyelitis | Pus and blood, excess of bladder epithelium (varies with cause and complication). |
| Cystitis, Chronic . . (untreated) . . . | — ammoniacal "ropy" | pale | low | abs. — | ditto | Very turbid. Bacteria. Crystals of ammonium urate, triple phosphate, disintegrated pus corpuscles. Blood and bladder epithelium. |
| (treated) . . . . | — usually acid, not ropy | pale | low | . . . . . | ditto | Pus, blood, and bladder epithelium. |

# APPENDIX C.

## TABULAR ARRANGEMENT OF HELLER'S CHEMICAL TESTS.

### Physical Properties.

*Color.* — Pale, normal, high, or dark.

*Odor.* —

*Reaction.* — Acid, neutral, or alkaline.

*Sp. gr.* — By urinometer.

*Sediment.* — Slight, considerable, or much.

### Normal Constituents.

*Urophœine* (Uph.). — $H_2SO_4$ + double quantity of Ur. = immediate brown color.

*Indoxyl* (Ixl.). — HCl + 3 gtt. $HNO_3$ + 30 gtt. Ur. = amethyst color.

*Urea* (Ū). — 1 gtt. Ur. + 1 gtt. $HNO_3$ in wgl. = nit. urea cryst. in 20 to 30 minutes.

*Uric Acid* (Ū). — ½ tt. Ur. + HCl = Ū cryst. in 24 hours.

*Chlorine* (Cl). — Ur. + $HNO_3$ + $AgNO_3$ (1:8) = solid ball of Ag Cl, if normal.

*Sulphates* (Sf) — ½ tt. Ur. + $BaCl_2$ sol. (sat. sol. + ⅛ HCl) = Ppt. (½ concav. of tt.).

*Earthy Phosphates* (E. P.). — ½ tt. Ur. + $NH_4OH$ = Ppt. ¼ to ½ in. in tt., if normal.

*Alkaline Phosphates* (A. P.). — Filtrate from E. P. + $MgSO_4$ sol. (sat. sol. $MgSO_4$ + $NH_4Cl$) = Ppt. ½ to ¾ in. in tt., if normal.

### Abnormal Constituents.

*Albumen* (Alb.) — Heat or $HNO_3$ = Coagulum or zone.

*Bile Pigments.* — Ur. spread on plate + 1 gtt. $HNO_3$ = prismatic rings.

*Sugar.* — Ur. in tt. + NaOH + $CuSO_4$ + heat = Ppt. yellow ($Cu_2O$).

*Sediment.* — Let settle and examine by microscope.

Experience will show that, in performing these tests, it is more convenient to examine for albumen immediately after urophæine and indoxyl; for if present in any considerable amount, albumen must be removed in order that its presence shall not interfere with the proper reaction of the subsequent tests.

The nitric acid test for albumen abridges several other tests, viz.: —

A zone above the junction of the urine and acid, *in the urine*, indicates an excess of urates and uric acid. A zone below the junction, *in the acid*, indicates the presence of nitrate of urea, hence an excess of urea.

If bile pigment is present, the characteristic play of colors will be observed.

The presence of iodine is indicated by a fine brown granular zone where the albumen zone is usually found, i. e. between the urine and acid.

Finally, if the amount of albumen present is small, the chlorides may be tested for in the same glass, after the above determinations have been made, by first stirring the urine and acid together with a glass rod, and then adding a drop of $AgNO_3$.

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